KU Leuven
Groep Biomedische Wetenschappen
Faculteit Geneeskunde
Departement Beeldvorming en Pathologie

DOCTORAL SCHOOL
BIOMEDICAL SCIENCES

OMFS
IMPATH

GROEI-BEINVLOEDING VAN HET GELAAT
BIJ KINDEREN MET EEN SKELETALE KLASSE III AFWIJKING

Joeri MEYNS

Jury:

Promotor: Prof. Dr. Reinhilde Jacobs
Copromotor: Prof. Dr. Constantinus Politis

Voorzitter leescommissie: Prof. Dr. Jan Verbakel
Voorzitter openbare verdediging: Prof. Dr. Koen Van Laere

Juryleden: Prof. Dr. Maria Cadenas de Llano Perula
Dr. Theo Hoppenreijs
Prof. Dr. Ivo Lambrichts
Prof. Dr. Johan Lammens
Dr. Aly Medhat

Proefschrift voorgedragen tot het behalen van de graad van Doctor in de Biomedische Wetenschappen

Mei 2025

KU Leuven
Biomedical Sciences Group
Faculty of Medicine
Department of Imaging and Pathology

DOCTORAL SCHOOL
BIOMEDICAL SCIENCES

FACIAL GROWTH MODIFICATION
IN CHILDREN WITH SKELETAL CLASS III MALOCCLUSION

Joeri MEYNS

Jury:

Promotor: Prof. Dr. Reinhilde Jacobs
Copromotor: Prof. Dr. Constantinus Politis

Chair Examining committee: Prof. Dr. Jan Verbakel
Chair public defense: Prof. Dr. Koen Van Laere

Jury members: Prof. Dr. Maria Cadenas de Llano Perula
Dr. Theo Hoppenreijs
Prof. Dr. Ivo Lambrichts
Prof. Dr. Johan Lammens
Dr. Aly Medhat

Dissertation presented in partial fulfilment of the requirements for the degree of Doctor in Biomedical Sciences

May 2025

Dissertation presented in partial fulfilment of the requirements for the degree of Doctor Biomedical Sciences.

PREFACE

This doctoral thesis consists of an introduction, seven research papers and a conclusion. The chapters were based on following peer-reviewed publications and manuscripts.

Chapter 3 — Meyns J., Brasil D.M., Mazzi-Chaves J.F., Politis C., Jacobs R. The clinical outcome of skeletal anchorage in interceptive treatment (in growing patients) for class III malocclusion: a systematic review.
Int J Oral Maxillofac Surg 2018; 47: 1003–1010

Chapter 4 — Van Hevele J, Nout E, Claeys T, Meyns J, Scheerlinck J, Politis C. Bone-anchored maxillary protraction to correct a class III skeletal relationship: A multicenter retrospective analysis of 218 patients.
Journal of cranio-maxillofacial Surgery 2018; 46: 1800-180

Chapter 5 — Meyns J., Meewis J., Dons F., Schreurs A., Aerts J., Shujaat S, Politis C., Jacobs R. Long-term Comparison of Maxillary Protraction with Hybrid Hyrax-Facemask vs Hybrid Hyrax-Mentoplate Protocols Using Alt-RAMEC: A 5-Year Randomized Controlled Trial
European Journal of Orthodontics, 47(2), April 2025.

Chapter 6 — Meyns J., Jindanil T., Shujaat S., Politis C., Jacobs R. Long-term Three-dimensional Skeletal Effects of Hybrid Hyrax with Facemask versus Mentoplate in Growing Class III Patients: A Randomized Controlled Trial.
Progress in Orthodontics, 26 (14) April 2025

Chapter 7 — Meyns J., Van Caesbroeck K., Jazil O., Jindanil T., Shujaat S., Politis C., Jacobs R. Comparing Long-term outcomes of Facemask versus Mentoplate therapy in class III malocclusion: a 5-year follow-up study. *Under review with Plos One*

Chapter 8 — Meyns J., Vertenten W., Shujaat S., Van Cauter S., Politis C., Vander Sloten J., Jacobs R. Evaluating the Predictive Potential of Patient-Specific Biomechanical Models in Class III Protraction Therapy. *Under Review with Clinical Oral invest*

“We do not receive wisdom, we must discover it for ourselves, after a journey through the wilderness which no one else can make for us, which no one can spare us, for our wisdom is the point of view from which we come at last to regard the world.”

M.Proust

ACKNOWLEDGEMENTS

Een PhD komt niet tot stand zonder de hulp van anderen en is het resultaat van een zevenjarig avontuur. Dit traject begon vanuit een klinische vraagstelling en een vaststelling bij de patiënten die ik behandelde. Misschien was het in 2018 een impulsieve beslissing om deze weg in te slaan – zonder enig idee welke uitdagingen me te wachten stonden. Maar al snel merkte ik dat dit pad onmogelijk alleen te bewandelen is. Samenwerking, aanmoediging en steun bleken essentieel. Daarom wil ik iedereen ontzettend hard bedanken voor de onschatbare steun in de afgelopen jaren.

Mama en papa, dank jullie wel voor het creëren van een warm nest. Ook al maakte ik niet altijd de meest evidente keuzes, jullie hebben mij altijd onvoorwaardelijk gesteund in alles wat ik ondernam. Zonder jullie had ik hier nooit gestaan. Ook **Benny, Tineke, Elena en Amelie**, bedankt voor alle fijne familiemomenten en jullie steun.

Mijn dank gaat ook uit naar mijn schoonfamilie, **Nico en Geert**, die al meer dan twintig jaar als een tweede thuis voor mij voelen. Onze gezellige familiemomenten, samen met **Victor en Simon**, zorgen altijd voor warmte en energie om weer verder te gaan. De afgelopen jaren waren helaas niet altijd makkelijk, en het gemis van **Katja en Paula** is groot. Maar hun eeuwige optimisme en sterke persoonlijkheden blijven een bron van moed en inspiratie om door te zetten.

Aan mijn **vrienden**, die niet altijd begrepen waarom ik op dit punt in mijn leven nog steeds de "eeuwige student" was: bedankt voor alle mooie momenten die lichtpuntjes waren in mijn soms overvolle agenda.

Aan mijn **collega's van het ZOL** – Serge, Sarah, Guido, Olivier en Griet – dank voor jullie steun en het creëren van een werkomgeving waarin het mogelijk was om dit doctoraat af te ronden. Dit project slokte vaak mijn aandacht en tijd op, maar ik heb nooit een woord van kritiek gehoord. Dat waardeer ik enorm. Ook aan alle **medewerkers in het ZOL** wens ik mijn oprechte dank uit te drukken. Jullie

onuitputtelijke enthousiasme, dagelijkse inzet, grappige intermezzo's en collegiale sfeer creëren een omgeving waarin het fijn is om te werken en waar geen moment saai is.

Prof. Dr. Reinhilde Jacobs, u was een onmisbare pilaar tijdens deze reis. Uw passie, geduld, oplossingsgerichte mindset, creativiteit en inzichten waren van onschatbare waarde. U bracht de juiste mensen samen en faciliteerde samenwerkingen die dit project mogelijk maakten. Deel uitmaken van de **OMFS-IMPATH-groep** was een eer. Het is een thuis voor onderzoekers van over de hele wereld en biedt een vruchtbare bodem voor interessante projecten en boeiende samenwerkingen. Uw werkethiek, doorzettingsvermogen en zorgzame houding zijn voor mij een groot voorbeeld.

Prof. Dr. Constantinus Politis, wij kennen elkaar al van vóór dit doctoraat. Toen ik u voor het eerst over dit project sprak, moedigde u mij onmiddellijk aan en overtuigde u me om ervoor te gaan. Gedurende mijn hele carrière, ook buiten dit doctoraat, heeft u mij gesteund, en daar ben ik u ontzettend dankbaar voor. Uw passie en werkethos zijn ongeëvenaard en inspirerend.

Prof. Dr. Dr. Peter Kessler, in Maastricht ben ik onder uw vleugels gegroeid als chirurg, mede dankzij het vertrouwen dat u mij altijd hebt gegeven. De eerste mentoplates werden daar geplaatst, en u heeft mij altijd gesteund en de ruimte gegeven om mijn eigen weg te gaan. Zonder u was dit project nooit tot stand gekomen.

Prof. Dr. Sohaib Shujaat. thank you for your help and effort throughout the entire project. Although we only met in person a few times, it feels like we have known each other for a long time. The amount of work you have put into all the projects is enormous. You were always there to provide advice, offer new insights, and analyze statistics. Your proofreading skills are exceptional, and without your help, I could not have completed this journey.

Veel dank aan de **orthodontisten** die meewerkten aan deze studie en voor het nauwkeurig uitvoeren van de orthodontische behandelingen bij deze patiënten. Een speciale dank aan **Arnoud Schreurs** voor jouw toewijding en enthousiasme in de afgelopen jaren. Zonder jullie allen was dit niet mogelijk geweest.

Ik wil ook alle **onderzoekers** bedanken met wie ik de afgelopen jaren heb samengewerkt. Dit was een echt groepsproject, en zonder hun inzet en bijdrage had dit project nooit tot stand kunnen komen.

Thanatchaporn Jindanil, thank you for your unwavering dedication during those countless drives from Leuven to Genk in the Cambio car—often for just a single patient. Your persistence and patience have been truly remarkable, and without them, this thesis would not have been possible.

Dank ook aan **Jeroen Meewis** voor de aanhoudende inspanningen om patiënten te contacteren voor follow-up en samen met **Ellen Gielen** de planning van de CT-scan-afspraken te verzorgen. De snelheid en flexibiliteit waarmee jullie dit aanpakten, was werkelijk bewonderenswaardig.

Aan alle **juryleden**, bedankt voor jullie tijd en inspanningen om dit lijvige document kritisch door te nemen en te evalueren.

En dan, mijn allerliefste schat, **liefste Katrien**. Als er iemand is die ik moet bedanken voor onvoorwaardelijke steun, dan ben jij het wel. Wanneer ik weer eens in het weekend moest werken, avonden achter de computer verdween of vastzat in een online meeting, bleef jij me steunen. Je hebt mij – en onze tijd samen – met veel anderen moeten delen. Toch bleef je mij altijd aanmoedigen, ook als de moed mij in de schoenen zakte.

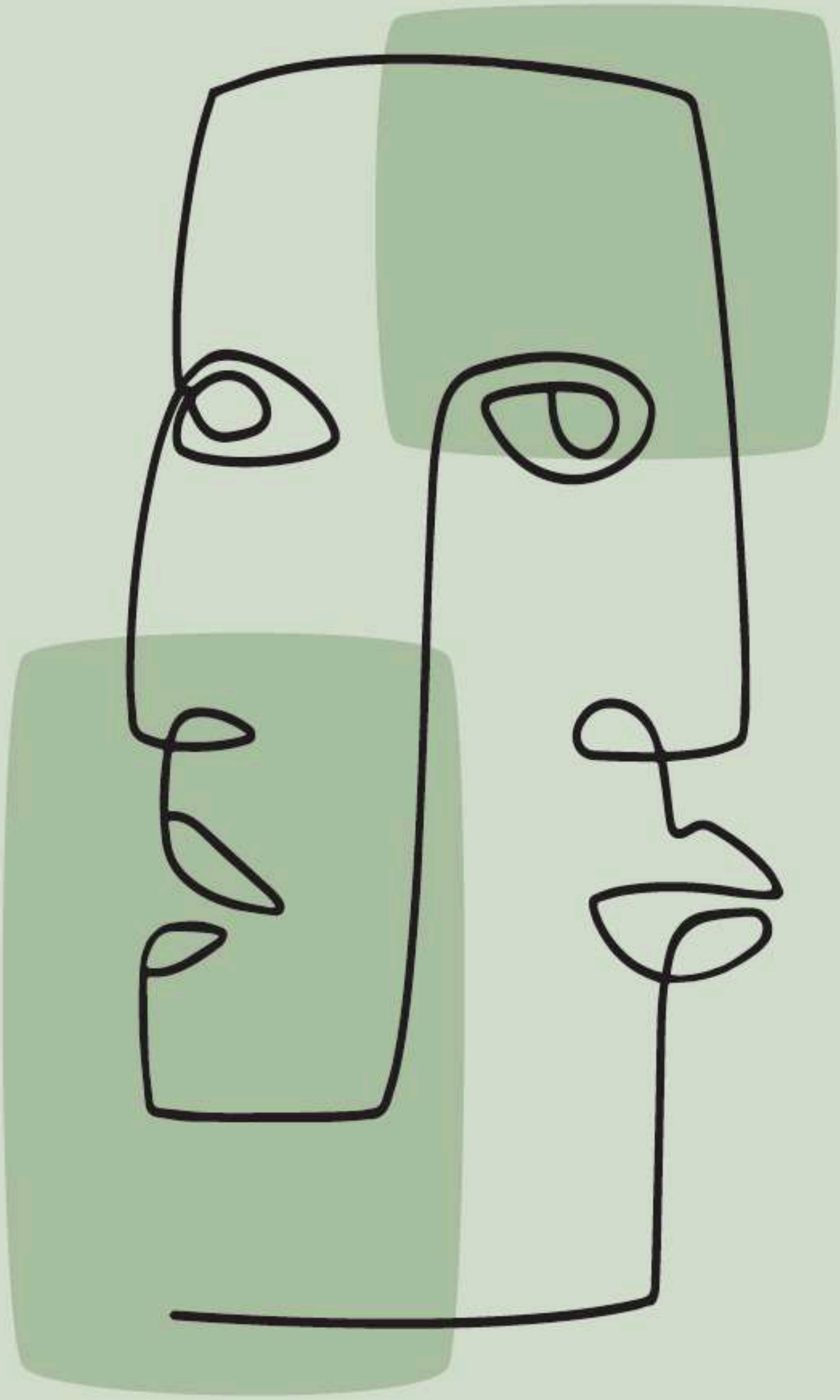
En tot slot, mijn andere lieve schatten, **Anna en Arthur**. Jullie hebben papa vaak moeten missen omdat hij weer eens achter die "stomme" computer zat voor dat project dat ik niet goed kon uitleggen – waarom, waarover en hoe het allemaal werkte. Maar weet dat dit avontuur nu voltooid is en dat ik nu weer volop tijd heb voor jullie.

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

2D	Two Dimensional
3D	Three Dimensional
AI	Artificial Intelligence
Alt-RAMEC	Alternate Rapid Maxillary Expansions and Constrictions
ANB	A point-Nasion-B point angle
BAFM	Bone Anchored Facemask Protraction
BAIP	Bone Anchored Intermaxillary Protraction
BAMP	Bone Anchored Maxillary Protraction
CBCT	Cone Beam Computed Tomography
CCT	Controlled Clinical Trial
CCW	Counterclockwise
CT	Computed Tomography
DICOM	Digital Imaging and Communications in Medicine
FE	Finite Element
FEA	Finite Element Analysis
FEM	Finite Element Model
FM	Facemask
GTVR	Growth Treatment Vertical Ratio
HH	Hybrid Hyrax
ICC	Intraclass Correlation Coefficient
IOFTN	Index of Orthognathic Functional Treatment Need
MP	Mentoplate
ODI	Overbite Depth Indicator
PCAmD	Part Comparison Analysis modeled Deformation
PCAaD	Part Comparison Analysis actual Deformation
RCT	Randomized Controlled Trial
Ret	Retrospective non-randomized clinical trial
RPE	Rapid Palatal Expansion
SA	Skeletal Anchorage
SD	Standard Deviation
SNA	Sella-Nasion-A point angle

SNB	Sella-Nasion-B point angle
SNO	Sella-Nasion-Orbitale angle
STL	Standard Tessellation Language
T0	Baseline timepoint
T1	One-year follow-up timepoint
T2	Five-year follow-up timepoint
TB	Tooth-Borne
TMJ	Temporomandibular Joint
VP	Virtual Patient



SECTION 1: General introduction, aims and hypothesis

CHAPTER 1

General introduction

Introduction: *“The long road to a Smile “.*

When 10-year-old Anna went to the orthodontist for the first time, her parents, Sarah and Tom, were nervous but hopeful. The persistent underbite had become increasingly noticeable over the years, and Anna’s teasing classmates weren’t making things easier. “Don’t worry, sweetheart,” Sarah whispered as they entered the clinic. “We’re going to get that fixed.”

The orthodontist, Dr. Patel, explained Anna’s condition: a Class III malocclusion caused by a growth discrepancy where her lower jaw was growing faster than her upper jaw. “It’s not uncommon, but we need to intervene early to guide her growth,” said Dr. Patel. He recommended interceptive treatment using bone anchorage: a minor procedure medically, but a significant and emotional journey for Anna and her parents.

Phase One: Hope and Excitement

A few weeks later, Anna began her journey. Bone anchors—tiny titanium plates and screws—were carefully inserted into her upper and lower jaws under general anesthesia. These anchors would provide a stable point to pull her upper teeth and jaw forward using elastic bands. It was a procedure that Sarah and Tom were initially apprehensive about, but Dr. Patel reassured them it was minimally invasive and crucial to Anna’s treatment.

Anna adapted quickly, although the first few days were tough. “It hurts a bit, but it’s not so bad,” she told her mum after school. Her parents were proud of her bravery, and the small victories—like seeing her teeth begin to align and her bite improve—lifted everyone’s spirits. By the time Anna was 12, her occlusion looked almost perfect. “She’s smiling more,” Tom noticed. “She looks so confident now.”

The family celebrated the milestone. They had followed every instruction, attended every appointment, and invested their hopes in the treatment.

Relapse: The shadows return

But as Anna grew older, the optimism began to fade. By the time she was 15, Sarah noticed subtle changes. Anna's lower jaw seemed to be "catching up". She was losing the harmonious profile they had worked so hard to achieve. Dr. Patel confirmed her fears: despite the success of the interceptive treatment, Anna's natural jaw growth was causing a relapse.

"It's no one's fault," Dr. Patel gently explained during the consultation. "In some cases, despite our best efforts, the lower jaw continues to grow disproportionately. We've reached a point where orthodontics alone might not be enough."

Anna, now a teenager, was devastated. "Why did we go through all this if it wasn't going to work?" she cried. Sarah and Tom were heartbroken but tried to remain strong. "This is just a setback," Tom said, although he too felt the weight of the years they had spent in treatment.

The Decision for surgery

By the time Anna was 18, the relapse had worsened. Her Class III malocclusion was not only affecting her appearance, but also her chewing and speech. Orthognathic surgery was now the only option to achieve a stable, functional bite. The news was daunting. "It's a big operation," admitted Dr. Patel. "But it can really change her life."

Anna was reluctant at first. The idea of surgery frightened her, and she was worried about how she would look afterward. Sarah and Tom spent countless nights talking through her fears, reassuring her that they would support her no matter what. "You've been so strong through all this," Sarah told her one night. "This is the last step."

The surgery and final chapter

The surgery was scheduled for the summer after Anna graduated from high school. The orthognathic surgery involved moving Anna's lower jaw back and her upper jaw forward to align them properly. It was a meticulous procedure that required weeks of recovery. The night before the operation, Anna held her parents' hands tightly. "I'm scared," she admitted. "But I just want it to be over."

The operation went smoothly, but the recovery was challenging. Anna had to deal with swelling, discomfort and a liquid diet for a few weeks. But slowly the swelling subsided and the results became clear: her profile was balanced, her bite was perfect, and her smile radiant.

Reflections and triumph

Today, Anna is a 20-year-old university student with a smile that lights up the room. Looking back, she's grateful for the journey, even though it wasn't without its emotional toll. "There were times I wanted to give up," she says. "But I'm glad I didn't. I feel like myself now."

For Sarah and Tom, the experience was a lesson in resilience and the importance of supporting their daughter every step of the way. "It has been a long road," says Sarah. "But to see her smile now, confident and happy—it was worth every moment."

This story highlights the experience of some patients undergoing class III interceptive treatment and the profound impact it can have on patients and their families.

Class III malocclusion

Prevalence and etiology

Class III malocclusion is one of the most challenging conditions in orthodontic practice, affecting approximately 0-26% of populations worldwide, with significant differences between ethnic groups. Chinese and Malaysian populations have higher rates of class III malocclusion, whereas Indian populations have lower rates [1]. This wide range can be attributed to differences between races, ethnic groups, and geographic regions [2] . This condition, characterized by either maxillary deficiency, mandibular excess, or a combination of both, can have a significant impact on both function and aesthetics. The complexity of Class III malocclusion lies not only in the variety of skeletal presentations, but also in the unpredictable nature of growth patterns and treatment responses.

When discussing Class III malocclusion, various subtypes can be identified, and terminology can sometimes be confusing. A distinction is often made between true (skeletal) Class III and pseudo (functional/dental) Class III malocclusion. It is critical to differentiate between dental and skeletal Class III in children, since dental Class III malocclusion typically does not require interceptive treatment. This differentiation in children is best determined through clinical examination, with radiographic analysis providing further clarification. While cephalometric analysis can aid in early diagnosis, it should be integrated into a comprehensive diagnostic approach that considers multiple developmental factors in young children.

Skeletal (true) Class III malocclusion is characterized by a maxillary deficiency combined with a large, prognathic mandible. In contrast, pseudo-Class III malocclusion involves a deficient maxilla with a normal mandible, caused by premature contact that leads to forward functional positioning of the mandible. The criteria for pseudo-Class III malocclusion remain poorly defined, and its dentoskeletal characteristics—particularly in the mixed dentition stage—are not well understood. Some classify pseudo-Class III malocclusion as a condition involving a normal mandible with a hypoplastic maxilla [3], while others describe it as a positional discrepancy resulting from an acquired neuromuscular reflex [4]. Given these ambiguities, the clinical assessment of occlusion and facial profile is of utmost importance in evaluating affected children. In this thesis, interceptive treatment is applied exclusively to skeletal Class III malocclusions. When referring to functional Class III malocclusion, we specifically mean dental or pseudo-Class III malocclusion.

The condition has a strong genetic component, with several patterns of inheritance: - Autosomal-recessive - Autosomal-dominant - Autosomal-dominant with incomplete penetrance - Polygenic threshold model [5]. The Habsburg dynasty is a famous historical example of this condition. Research shows that inbreeding particularly affected the lower third of the face, suggesting a recessive inheritance pattern of the "Habsburg jaw [6]. Genetic research has identified specific chromosomal regions (1p36, 12q23, 12q13) and genes associated with Class III malocclusion, including: - Indian hedgehog homolog (IHH) - Parathyroid-hormone like hormone (PTHLH) - Insulin-like growth factor-1 (IGF-1) - Vascular endothelial growth factor (VEGF) - Erythrocyte membrane protein band 4.1 (EPB41) [7].

While genetic factors are primary, environmental factors also play a role [8]. Several environmental factors can influence normal dental eruption patterns. Conditions such as retained deciduous teeth, odontomas, and dental trauma can lead to palatal eruption of upper incisors and labial eruption of lower incisors. These altered eruption patterns often cause premature occlusal contacts, potentially resulting in an anterior displacement of the mandible [9]. Additionally, early loss of lower second primary molars while the upper counterparts remain can allow lower first permanent molars to drift mesially into the Leeway space, ultimately disturbing the overall molar relationship [10].

Anterior crossbite may negatively impact maxillary growth; therefore, its early correction is advisable to prevent restriction of maxillary development. Common therapeutic approaches for correcting anterior crossbite include reverse headgear, removable appliances, and fixed orthodontic appliances. Children with non-nutritive sucking habits exhibit a higher prevalence of molar Class II relationships in females, whereas molar Class III relationships occur more frequently in males, compared to children without such habits [11].

There are notable differences in upper airway characteristics between patients with Class II and Class III malocclusions. Although the exact role of habits such as mouth breathing in the etiopathogenesis of malocclusions remains controversial, their presence alongside malocclusion is highly relevant to treatment prognosis. Therefore, addressing these issues is essential to establish a proper functional environment that promotes physiological growth [12]. Patients with Class II malocclusions commonly exhibit nasal obstruction and enlarged adenoids, whereas those with Class III malocclusions typically do not experience nasal obstruction and have a larger pharyngeal airway. In Class III patients, however, enlarged tonsils can significantly restrict the oropharyngeal space, pushing the tongue forward and causing anterior displacement of both mandibular incisors and the mandible. Consequently, interventions such as tonsillectomy or tongue posture correction may be indicated for Class III individuals with tonsillar hypertrophy and anterior tongue positioning, despite the absence of nasal obstruction [13].

Furthermore, research among Tanzanian children has shown a strong association between malocclusion prevalence, dental caries experience, and lower socioeconomic status. This suggests the importance of implementing preventive programs aimed at improving oral health outcomes in such communities [14].

Cultural differences and geographic variations may influence the condition's development, although specific environmental factors require further research [1,2,5]. Understanding these factors is essential for accurate diagnosis and effective treatment planning.

Treatment options

Treatment of Class III malocclusion has evolved significantly over the past century, from basic dental adjustments to advanced orthopedic techniques. Historically, Class III malocclusion was often considered synonymous with mandibular prognathism, regardless of the skeletal structures involved. This perspective led to a limited range of treatment options, primarily focused on managing mandibular growth. The standard approach was to wait until growth was complete before combining orthodontic treatment with orthognathic surgery. This strategy was based on the belief that mandibular growth, which is primarily determined by genetic factors, could not be effectively controlled by early orthodontic interventions [15]. A major breakthrough came with the recognition that maxillary development also plays a critical role in Class III malocclusions. This led to new treatment approaches, in particular the development of orthopedic devices designed to influence maxillary growth and position [16]. Key innovations include facemasks - combined with rapid maxillary expansion [17,18] -, chincups for mandibular growth control [18], functional appliances like the Frankel (FR-III) [19] and skeletal anchorage devices (miniplates and miniscrews) [18,20–22]. Conventional treatment approaches have relied primarily on facemask therapy, often combined with rapid maxillary expansion. Although this method has been shown to be effective, it has significant limitations, including dependence on patient compliance and potential dental side effects [23].

Expansion of the upper jaw can increase the skeletal response by loosening the circummaxillary sutures. Although the effectiveness of Rapid Palatal Expansion (RPE) for augmenting maxillary protraction is still debated, some studies suggest it may enhance skeletal effects by mobilizing midfacial sutures [23, 24]. The Alternate Rapid Maxillary Expansion and Constriction (Alt-RAMEC) protocol, involving repeated cycles of rapid expansion and constriction of the maxilla, further claims to achieve greater and faster skeletal changes, in part by stimulating upper jaw growth through more pronounced circummaxillary suture opening [25–27].

The development of skeletal anchorage systems over the past two decades has opened up new possibilities for Class III treatment, promising more direct skeletal effects and potentially better control over unwanted dental compensations. Early intervention during growth has been increasingly advocated to modify skeletal growth patterns and potentially reduce the need for surgical correction in adulthood. Advanced 3D imaging technology, particularly CBCT, has improved the accuracy of diagnosis and treatment planning. However, the timing and method of intervention remain subject of ongoing debate within the orthodontic community, while the long-term stability of early orthopedic treatment remains under investigation.[15,17,21,22].

Treatment outcome

Despite these advances, several critical questions remain unanswered and approximately 25 – 30 % of all patients could still benefit from orthognathic surgery after class III interceptive treatment [28–34] . The comparative effectiveness of traditional versus newer skeletal anchorage approaches lacks robust evidence from long-term randomized controlled trials [20–22]. In addition, the ability to predict treatment outcomes and identify patients most likely to benefit from early intervention remains limited, complicating clinical decision-making [35].

REFERENCES

1. Hardy DK, Cubas YP, Orellana MF. Prevalence of angle class III malocclusion: A systematic review and meta-analysis. *Open J Epidemiol*. 2012;02(04):75-82.
2. Zere E, Chaudhari PK, Sharan J, Dhingra K, Tiwari N. Developing Class III malocclusions: Challenges and solutions. *Clin Cosmet Investig Dent*. 2018;10(June):99-116.
3. Tweed CH. *Clinical Orthodontics*. C. V. Mosby; 1966.
4. Moyers RE. *Handbook of Orthodontics*. Year Book Medical Publishers; 1988.
5. Liliana M. Otero, Lorri Ann Morford, Gabriel Falcão-Alencar JKH; Family History and Genetics of Mandibular Prognathism,. In: *Orthodontic Treatment of Class III Malocclusion*. Vol 1. ; 2014.
6. Vilas R, Ceballos FC, Al-Soufi L, et al. Is the "Habsburg jaw" related to inbreeding? *Ann Hum Biol*. 2019;46(7-8):553-561.
7. Xue F, Wong RWK, Rabie ABM. Genes, genetics, and Class III malocclusion. *Orthod Craniofac Res*. 2010;13(2):69-74. doi:10.1111/j.1601-6343.2010.01485.x
8. Nowrin SA, Alam MK, Basri R. GENETIC EFFECT AND PREVALENCE OF CLASS III MALOCCLUSION IN DIFFERENT POPULATION: AN OVERVIEW. *Int J Pharma Bio Sci*. Published online 2015. https://api.semanticscholar.org/CorpusID:2090708
9. Lee BD. Correction of crossbite. *Dent Clin North Am*. 1978;22(4):647-668.
10. Rabie AB, Gu Y. Diagnostic criteria for pseudo-Class III malocclusion. *Am J Orthod Dentofacial Orthop*. 2000;117(1):1-9. doi:10.1016/S0889-5406(00)70241-1
11. Machado SCS, Manzanares-Céspedes MC, Ferreira-Moreira J, Ferreira-Pacheco JJ, Rompante PAMA, Ustrell-Torrent JM. A sample of non-nutritive sucking habits (pacifier and digit) in portuguese children and its relation with the molar classes of angle. *J Clin Exp Dent*. 2018;10(12):1161-1166.
12. Rodríguez-Olivos LHG, Chacón-Uscamaita PR, Quinto-Argote AG, Pumahualcca G, Pérez-Vargas LF. Deleterious oral habits related to vertical, transverse and sagittal dental malocclusion in pediatric patients. *BMC Oral Health*. 2022;22(1):1-7.
13. Iwasaki T, Sato H, Suga H, et al. Relationships among nasal resistance, adenoids, tonsils, and tongue posture and maxillofacial form in Class II and Class III children. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2017;151(5):929-940.
14. Mtaya M, Brudvik P, Åstrøm AN. Prevalence of malocclusion and its relationship with socio-demographic factors, dental caries, and oral hygiene in 12- to 14-year-old Tanzanian schoolchildren. *Eur J Orthod*. 2009;31(5):467-476.
15. Oltramari-Navarro PVP, de Almeida RR, Conti AC de CF, Navarro R de L, de Almeida MR, Fernandes LSFP. Early treatment protocol for skeletal Class III malocclusion. *Braz Dent J*. 2013;24(2):167-173.
16. Delaire J. [Treatment of Class III with dentofacial orthopedic mask]. *Acta Odontol Venez*. 1979;17(2-3):168-200.
17. Woon SC, Thiruvenkatachari B. Early orthodontic treatment for Class III malocclusion: A systematic review and meta-analysis. *Am J Orthod Dentofacial Orthop*. 2017;151(1):28-52.
18. Ngan P, Moon W. Evolution of Class III treatment in orthodontics. *Am J Orthod Dentofacial Orthop*. 2015;148(1):22-36. doi:10.1016/j.ajodo.2015.04.012
19. De Toffol L, Pavoni C, Baccetti T, Franchi L, Cozza P. Orthopedic Treatment Outcomes in Class III Malocclusion. *Angle Orthodontist*. 2008;78(3). doi:10.2319/030207-108.1
20. Rodríguez de Guzmán-Barrera J, Sáez Martínez C, Boronat-Catalá M, et al. Effectiveness of interceptive treatment of class III malocclusions with skeletal anchorage: A systematic review and meta-analysis. Bencharit S, ed. *PLoS One*. 2017;12(3):e0173875.

21. Meyns J, Brasil DM, Mazzi-Chaves JF, Politis C, Jacobs R. The clinical outcome of skeletal anchorage in interceptive treatment (in growing patients) for class III malocclusion. *Int J Oral Maxillofac Surg*. 2018;47(8):1003-1010.
22. Cornelis MA, Tepedino M, Riis NDV, Niu X, Cattaneo PM. Treatment effect of bone-Anchored maxillary protraction in growing patients compared to controls: A systematic review with meta-Analysis. *Eur J Orthod*. 2021;43(1):51-68.
23. Kim JH, Viana M a, Graber TM, Omerza FF, BeGole E a. The effectiveness of protraction face mask therapy: a meta-analysis. *Am J Orthod Dentofacial Orthop*. 1999;115(6):675-685. doi:10.1016/S0889-5406(99)70294-5
24. Foersch M, Jacobs C, Wriedt S, Hechtner M, Wehrbein H. Effectiveness of maxillary protraction using facemask with or without maxillary expansion: a systematic review and meta-analysis. *Clin Oral Investig*. 2015;19(6):1181-1192.
25. Masucci C, Franchi L, Giuntini V, Defraia E. Short-term effects of a modified Alt-RAMEC protocol for early treatment of Class III malocclusion: A controlled study. *Orthod Craniofac Res*. 2014;17(4):259-269. doi:10.1111/ocr.12051
26. Pithon MM, De N, Santos L, et al. Is alternate rapid maxillary expansion and constriction an effective protocol in the treatment of Class III malocclusion? A systematic review Is alternate rapid maxillary expansion and constriction protocol effective in the treatment of Class III maloc- c. *Dental Press J Orthod Dental Press J Orthod Dental Press J Orthod*. 2016;212121(666):34-4234.
27. Ergul T, Gulec A. Comparison of the effectiveness of skeletal and tooth-borne protraction methods with or without alternate rapid maxillary expansion and constriction protocol in patients with Class III malocclusion. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2024;article in. doi:10.1016/j.ajodo.2024.10.010
28. Hagg U, Tse A, Bendeus M, Rabie ABM. Long-term follow-up of early treatment with reverse headgear. *Eur J Orthod*. 2003;25:95-102.
29. Baccetti T, Franchi L, McNamara JA. Treatment and posttreatment craniofacial changes after rapid maxillary expansion and facemask therapy. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2000;118(4):404-413.
30. Wells AP, Sarver DM, Proffit WR. Long-term efficacy of reverse pull headgear therapy. *Angle Orthodontist*. 2006;76(6):915-922.
31. Masucci C, Franchi L, Defraia E, Mucedero M, Cozza P, Baccetti T. Stability of rapid maxillary expansion and facemask therapy: A long-term controlled study. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2011;140(4):493-500.
32. Gebeile-Chauty S, Perret M, Schott AM, Aknin JJ. [Early treatment of Class III: a long-term cohort study]. *Orthod Fr*. 2010;81(3):245-254.
33. Mandall N, Aleid W, Cousley R, et al. The effectiveness of bone anchored maxillary protraction (BAMP) in the management of class III skeletal malocclusion in children aged 11–14 years compared with an untreated control group: A multicentre two-arm parallel randomised controlled trial. *J Orthod*. Published online 2024.
34. Mandall N, Cousley R, Dibiase A, et al. Early class III protraction facemask treatment reduces the need for orthognathic surgery: a multi-centre, two-arm parallel randomized, controlled trial. *J Orthod*. 2016;43(May 2017):164-175. doi:10.1080/14653125.2016.1201302
35. Fudalej P, Dragan M, Wedrychowska-Szulc B. Prediction of the outcome of orthodontic treatment of Class III malocclusions-a systematic review. *Eur J Orthod*. 2011;33(2):190-197. doi:10.1093/ejo/cjq052

CHAPTER 2

Hypothesis and aims

The introduction outlines the current landscape of research and knowledge on interceptive treatment for skeletal class III malocclusion. It presents significant challenges for surgeons, orthodontists, patients, and their parents. Several questions remain regarding timing and method of intervention, long term stability, long term treatment outcome and predictive tools.
This doctoral thesis examines the factors that influence the success of early treatment of skeletal Class III malocclusion. The research challenges the assumption that the type of treatment is the primary determinant of outcome.

Section 2: *Evaluating the efficacy of bone-anchors in class III interceptive treatment.*

Aim

1. Examine the effectiveness of more invasive treatments—such as bone anchors—by reviewing existing evidence on both short- and long-term outcomes.
2. Retrospectively analyze and measure the results of routine clinical practice over recent years.

Hypothesis:
Despite their invasive nature, using bone anchors in protraction therapy for skeletal Class III may not necessarily produce greater treatment effects compared to conventional approaches.

Chapter 3: Bone anchor efficacy in class III interceptive treatment.
Meyns J, Brasil D., Mazzi- Chaves J., Politis C, Jacobs R. The Clinical outcome of skeletal anchorage in interceptive treatment (in growing patients) for class III malocclusion, A systematic review. Int. J. Oral Maxillofac Surg, 2018; 47: 1003 – 1010

Chapter 4: Bone anchor efficacy in routine clinical practice.

Van Hevele J, Nout E, Claeys T, Meyns J, Scheerlinck J, Politis C. Bone-anchored maxillary protraction to correct a class III skeletal relationship: multicenter retrospective analysis of 218 patients. Journal of cranio-maxillofacial Surgery 2018; 46: 1800-1806.

Section 3: *Facemask treatment vs Mentoplate treatment protocol. A 5 year randomized controlled Trial.*

Aim

This section investigates the impact of bone anchorage on skeletal effects, dental compensations, and vertical control. By addressing a shortage of high-quality, long-term randomized controlled trials (RCTs) on Class III protraction, this research compares facemask therapy with bone-anchored protocols, evaluating both short-term and long-term outcomes using two-dimensional (2D) and three-dimensional (3D) measurements.

Hypothesis

Bone anchorage may yield greater skeletal effects, reduced dental compensations, and improved vertical control over both the short and long term.

Chapter 5: Overall two-dimensional assessment, comparison with existing evidence.

Meyns J., Meewis J., Dons F., Schreurs A., Aerts J., Shujaat S, Politis C., Jacobs R. Long-term Comparison of Maxillary Protraction with Hybrid Hyrax-Facemask vs Hybrid Hyrax-Mentoplate Protocols Using Alt-RAMEC: A 5-Year Randomized Controlled Trial. European Journal of Orthodontics Vol 47 (2) April 2025

Chapter 6: Overall three-dimensional assessment.

Meyns J., Jindanil T., Shujaat S., Politis C., Jacobs R. Long-term Three-dimensional Skeletal Effects of Hybrid Hyrax with Facemask versus Mentoplate in Growing Class III Patients: A Randomized Controlled Trial. Progress in Orthodontics, 26 (14) April 2025.

Section 4: *Treatment outcome prediction.*

Aim

1. Identify positive and negative predictive factors for treatment outcomes.
2. Investigate the predictive potential of patient-specific biomechanical models.

Hypothesis

Preoperative predictive factors can be identified in young Class III patients, and three-dimensional patient-specific models can offer insights into likely treatment outcomes.

Chapter 7: Two-dimensional analysis for Predicting Class III Malocclusion Treatment Outcomes.

Meyns J., Van Caesbroeck K., Jazil O., Jindanil T., Shujaat S., Politis C., Jacobs R. Comparing Long-term outcomes of Facemask versus Mentoplate therapy in class III malocclusion: a 5-year follow-up study. Under review with Plos One.

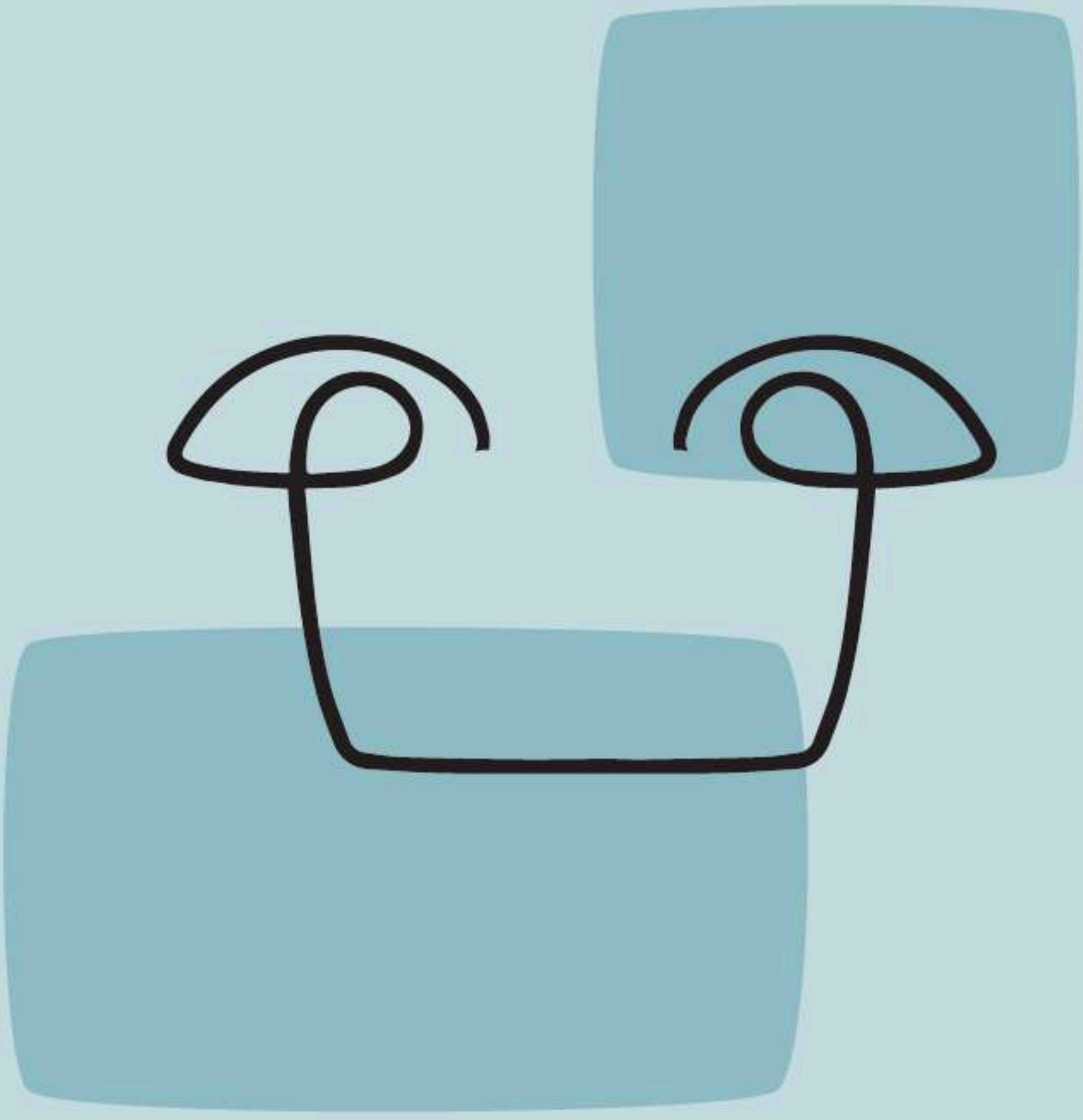
Chapter 8: Three-dimensional analysis for Predicting Class III Malocclusion Treatment Effect.

Meyns J., Vertenten W., Shujaat S., Van Cauter S., Politis C., Vander Sloten J., Jacobs R. Evaluating the Predictive Potential of Patient-Specific Biomechanical Models in Class III Protraction Therapy. Under Review with Clinical Oral invest.

Through this research, we aim to provide evidence-based guidance for clinical decision-making in Class III treatment, particularly regarding the choice between conventional and skeletal anchorage approaches. The findings will contribute to our understanding of treatment efficacy, stability and factors influencing long-term outcomes.

The thesis is organized to progressively deepen our understanding, beginning with a systematic review of existing evidence, proceeding with a clinical trial that assesses both immediate and long-term treatment outcomes, and concluding with biomechanical analyses and the exploration of potential predictive tools. This comprehensive approach allows us to consider not only the immediate effectiveness of different treatment modalities, but also their long-term stability and implications for future treatment needs.

By combining systematic review methodology, clinical trials, and biomechanical analysis this research provides a multi-faceted examination of Class III treatment approaches, offering insights that can guide clinical practice and future research directions in this challenging area of orthodontics.



SECTION 2: Bone anchor efficacy

CHAPTER 3

Bone anchor efficacy in class III interceptive treatment

This chapter is based on the following manuscript.

Meyns J, Brasil D., Mazzi- Chaves J., Politis C, Jacobs R. The Clinical outcome of skeletal anchorage in interceptive treatment (in growing patients) for class III malocclusion, A systematic review. Int. J. Oral Maxillofac Surg, 2018; 47: 1003 – 1010

ABSTRACT

A systematic review of the literature was performed regarding the clinical outcome (effectiveness) of bone anchorage devices in interceptive treatment for class III malocclusion. A search of Embase, PubMed and Web of Science databases yielded 285 papers. An additional 2 articles were retrieved trough manual searching of the reference lists. After initial abstract selection 32 potentially eligible articles were screened in detail, resulting in a final number of eight articles included in this review. Insufficient evidence was found regarding the effects of skeletal anchorage in interceptive class III treatment to support definitive conclusions on long term skeletal effects and stability.

In the short term it seems that bone-anchors can provide more skeletal effect with less dento-alveolar compensations and less unwanted vertical changes. This does not always exclude the use of a facemask. The use of miniscrews as skeletal anchorage device does not seem to provide more skeletal effect, although it could minimize the unwanted dental effects in the upper jaw. No information regarding the need for orthognathic surgery, orthodontic treatment time or patient compliance and complications was found in the selected articles.

INTRODUCTION

Class III malocclusions are considered to be among the most challenging orthodontic problems. It can be caused by either the upper jaw being too small, the lower jaw being too large, or a combination of both [1].The patient's age and growth stage are decisive factors in treating this craniofacial disharmony. At younger age orthopedic treatments are advocated to reduce the need of treatment in the permanent dentition. A series of treatment approaches can be found in the literature regarding orthopedic treatment in class III malocclusion [1–3]. Ellis and McNamara [4] found that 65% to 67% of all class III malocclusions were characterized by maxillary deficiency. Therefore, most treatment modalities rely on maxillary protraction. The principle of maxillary protraction is to apply an anteriorly directed force on the circummaxillary sutures, which are still patent at an early age and thereby stimulate bone apposition in the suture areas. Classically the force is transferred to the upper jaw through a tooth-borne device bonded to the maxillary teeth.

In recent years a number of techniques for orthopedic treatment with skeletal anchorage were popularized [5–19]. The use of miniplates and miniscrews would produce more skeletal effect and less (unwanted) dentoalveolar changes [10,19,20]. It could also have less unwanted counterclockwise rotation of the maxilla and clockwise rotation of the mandible, which is not desired in a high angle vertical growth pattern[2,6,11,21–27]. Most articles report follow-up in 2D cephalometric measurement. The ANB and Wits appraisal are key parameters for the diagnosis of skeletal class III malocclusion.[28]. However, the use of ANB has been questioned since it is sensitive to the position of the anterior cranial base and may vary according to the divergence of the jaws [29,30]. This is also the case with Wits appraisal, which can be affected by the cant of occlusal plane and by its variations due to tooth eruption[28]. The advances in 3-dimensional (3D) imaging of facial structures have provided alternative tools to analyze skeletal changes [31,32].

Although recent research has provided sufficient evidence for the successful use of interceptive treatment for class III malocclusion [3], there is still no consensus about the beneficial effect of the use of skeletal anchorage. The aim of the present review is to systematically analyze the scientific literature regarding the clinical outcome of skeletal anchorage in interceptive treatment of class III malocclusions.

MATERIAL AND METHODS

Search strategy

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines were followed to ensure the transparency and comprehensiveness of this systematic review [33]. A search protocol was specified in advance and registered at PROSPERO (international prospective register of systematic reviews) nr CRD42017076499.

The search strategy was developed for PubMed and appropriately modified for EMBASE and Web of Science. The electronic databases were searched through in august 2017. The full search protocol for the different databases is given in Table 3.1. English literature was searched and there was no restriction regarding publication date. Additionally, all references to earlier systematic reviews and selected full-text articles were manually screened for potentially useful articles. The objective was to determine the additional effects of skeletal anchorage in interceptive treatment for class III malocclusions on the following outcome measures: (1) better intermaxillary relationship (more skeletal effect and less dento-alveolar changes), (2) improvement in overjet and overbite, (3) less clockwise rotation of the mandible, (4) need for orthognathic surgery, (5) orthodontic treatment time, (6) patient compliance, and (7) complications.

Table 3.1: Search strategy

	Search strategy
Embase (Embase and Medline)	[Concept 1]: Patients with Class III malocclusion: 'malocclusion'/exp OR 'class III malocclusion*':ti,ab OR 'jaw malocclusion':ti,ab OR 'jaw occlusion disorder':ti,ab OR 'retrognathia'/exp OR 'receding jaw':ti,ab OR 'retrognathism':ti,ab; [Concept 2]: Orthop(a)edic treatment: 'removable orthodontic appliance'/exp OR 'removable orthodontic appliance*':ti,ab OR 'removable orthodontic device*':ti,ab OR 'functional orthodontic appliance'/exp OR 'functional orthodontic device*':ti,ab OR 'functional orthodontic appliances*':ti,ab OR 'orthodontic device'/exp OR 'activator appliance*':ti,ab OR 'orthodontic device*':ti,ab OR 'reverse-pull headgear'/exp OR 'reverse-pull headgear':ti,ab OR 'extraoral traction appliance*':ti,ab OR 'multi-adjustable facemask':ti,ab; [Concept 3]: Skeletal anchorage: 'orthodontic anchorage'/exp OR 'orthodontic anchorage*':ti,ab OR 'orthodontic anchorage procedure*':ti,ab OR 'bone screw'/exp OR 'bone screw*':ti,ab OR 'leibinger':ti,ab OR 'reimer screw*':ti,ab OR OR 'bone plate'/exp OR 'bone plate*':ti,ab OR 'bone plate device*' OR 'fixation plate*':ti,ab OR 'NCB':ti,ab
Web of Science	[Concept 1]: Patients with Class III malocclusion: Class III malocclusion* OR Ha?sburg Jaw OR mandibular prognathism OR Angle class III OR underbite OR retrognathia* OR skeletal class III OR mandibular hyperplasia OR maxillary retrusion OR maxillary hypoplasia OR mandibular protrusion; [Concept 2]: Orthop(a)edic treatment: orthodontic appliances, removable* OR orthodontic appliances, functional* OR frankel function regulator OR bimler appliance* OR kinetikor* OR activator appliance* OR activator orthodontic appliance* OR function activator* OR jasper jumper OR bionator* OR extraoral traction appliances* OR orthodontic headgear* OR orthodontic chincap* OR orthodontic face bow*; [Concept 3]: Skeletal anchorage: orthodontic anchorage procedures OR orthodontic anchorage technique* OR bone screw* OR bone plate* OR skeletal anchorage
Pubmed	[Concept 1]: Patients with Class III malocclusion: "Malocclusion, Angle Class III"[Mesh] OR Class III malocclusion*[tiab] OR Habsburg Jaw[tiab] OR mandibular prognathism[tiab] OR Angle class III[tiab] OR Hapsburg jaw[tiab] OR underbite[tiab] OR "Retrognathia"[Mesh] OR retrognathia*[tiab] OR skeletal class III[tiab] OR mandibular hyperplasia[tiab] OR maxillary retrusion[tiab] OR maxillary hypoplasia[tiab] OR mandibular protrusion[tiab]; [Concept 2]: orthop(a)edic treatment: "Orthodontic Appliances, Removable"[Mesh] OR removable orthodontic appliance*[tiab] OR "orthodontic appliances, functional" [MesH] OR Functional orthodontic appliance*[tiab] OR Frankel function regulator[tiab] OR Bimler appliance*[tiab] OR kinetor*[tiab] OR "Activator appliances"[MeSH] OR activator appliance*[tiab] OR Activator[tiab] OR Activator orthodontic[tiab] OR Activator orthodontic appliance*[tiab] OR Function activator* [tiab] OR Jasper jumper[tiab] OR bionator* [tiab] OR "Extraoral traction appliances"[MeSH] OR extraoral traction appliance*[tiab] OR extraoral traction[tiab] OR extra oral traction[tiab] OR Orthodontic headgear* [tiab] OR Orthodontic chincap*[tiab] OR chincap[tiab] OR chincup[tiab] OR orthodontic face bow*[tiab] OR facemask*[tiab] OR Face mask*[tiab] OR reverse pull headgear[tiab] OR Delaire mask[tiab] OR Delaire facial mask[tiab]; [Concept 3]: skeletal anchorage: "Orthodontic Anchorage Procedures"[Mesh] OR orthodontic anchorage procedure*[tiab] OR orthodontic anchorage technique*[tiab] OR "Bone Screws"[Mesh:NoExp] OR bone screw*[tiab] OR "Bone Plates"[Mesh] OR bone plate*[tiab] OR skeletal anchorage[tiab] OR mentoplate[tiab] OR bone anchored maxillary protraction[tiab] OR bone anchor[tiab] OR anchor[tiab]

The titles and abstracts of relevant studies identified through the electronic searches were screened by two authors (DB and JC). Full text articles were obtained of the studies that fulfilled the inclusion criteria. These full-text articles, together with the full-text articles found through the manual search were independently assessed by these authors to determine if they met the inclusion criteria. Disagreements were resolved by discussion. If, following a discussion, it was still unclear whether an article should be included, a third author (JM) was consulted. After selection, the data extraction and risk of bias assessment were performed.
Articles were included when (1) they reported on interceptive treatment for class III malocclusions with the use of skeletal anchorage (miniplates and/ or screws) compared to conventional class III treatment, (2) the full text was available in English language, and (3) they reported randomized clinical trials (RCTs), prospective non-randomized clinical trials (CCT) and retrospective non-randomized clinical trials (Ret), case-control studies, cohort studies and case series (10 or more patients). Exclusion criteria were articles reporting on non-growing class III or syndromal patients.

Data extraction and management

The data extraction was performed by two researchers (DB and JC) and supervised by two other authors (JM and RJ). If data was missing in the potentially eligible articles, the authors were contacted for clarification. The following data were recorded: (1) methods: study design, location, number of centers, recruitment period and funding source, (2) participants: inclusion and exclusion criteria, demographics, number of participants, (3) intervention: details regarding the type of intervention groups and materials used, and (4) outcomes: outcome measurements and follow-up.

Risk of bias assessment

The risk of bias assessment was performed according to the Cochrane Handbook for Systematic Reviews of Interventions, Chapter 8: Assessing risk of bias[34]. Two authors (DB and JC) independently performed the risk of bias assessment. Any disagreement was resolved by discussion or through consultation with a third author (JM). A judgement was expressed as 'low risk', 'high risk' or 'unclear risk' of bias for different categories of bias (selection bias, detection bias, attrition bias, reporting bias and other bias). To ensure that good judgements were made, authors were contacted if data in the original article were missing. After performing this assessment, the overall risk of bias of the included articles was assessed. Studies were categorised as 'low risk of bias' (low risk of bias in all key domains), 'unclear risk of bias' (unclear risk of bias in one or more key domains) or 'high risk of bias' (high risk of bias in one or more key domains). (see also Table 3.2: Risk of bias summary)

RESULTS

Description of studies

After screening the titles and abstracts of 285 unique papers, 14 potential eligible articles were selected. Of the 14 potentially eligible articles)[6,10,11,15,17,19–21,35–40], 6 had to be excluded. All these studies had to be excluded because they didn't have a good control group (with conventional treatment)[10,11,15,21,36,39]. Also see Table 3.2. The entire selection process therefore resulted in a total of 8 articles [6,17,19,20,35,37,38,40]. A flowchart of the literature search and selection process through the different stages of the systematic review (PRISMA) is given in Figure 3.1.

Table 3.2

Excluded articles with reasons	
Author (year)	Reason
Bozkaya et al (2017)[10]	1
Coscia et al (2012)[39]	1
Elnagar et al (2016)[21]	1
Kaya et al (2011)[15]	1
Kircelli et al (2008)[36]	1
Sar et al (2014)[11]	1

Legend: (1) no control group with conventional treatment

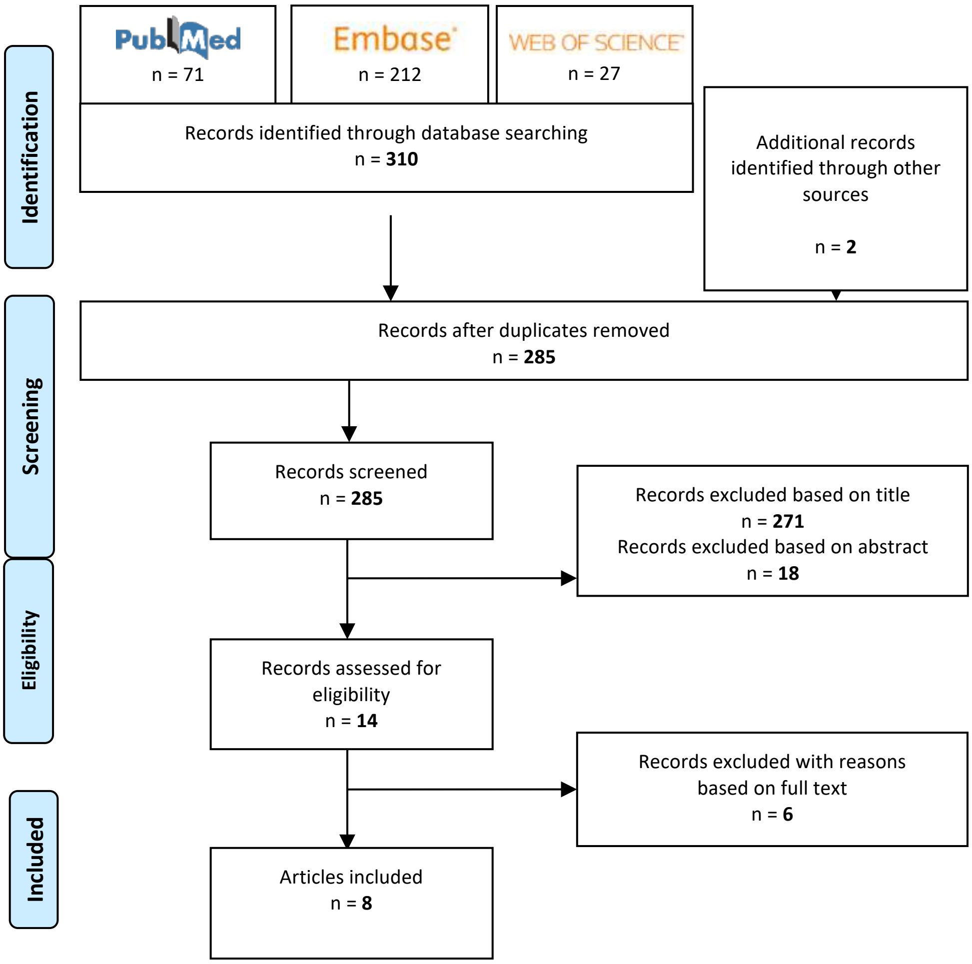


Figure 3.1: Flow diagram of the selection process (PRISMA 2009 format).

Characteristics of the trial settings and investigators

Of The 8 included studies, two were performed in Turkey [19,38] , one in Iran [35], one in Korea [17] and one in Taiwan [41] . Three studies were multicenter studies of which one was carried out in USA and Belgium[6], One in Brazil and Belgium [20] and one in USA and Germany[37]. Of the 8 studies, 5 were case control studies and 3 were a controlled clinical trial [19,38,41]. Seven studies did not report any funding or conflict of interest and one article reported no competing interests [37].

Characteristics of participants

The mean age of participants at start of treatment ranged from 8.1 to 11.2 years in the conventional treatment group and from 9.6 to 11.9 years in the skeletal anchorage group. All articles reported the mean age and the age range, except for one article which did not report the age range [41]. The distribution of boys and girls was reported in all studies. Between 10 and 25 patients were selected for the skeletal treatment and between 10 to 34 for the conventional treatment for each study. In total 304 patients were treated of which 149 patients were treated with conventional methods and 155 with skeletal anchorage. Although probably 2 articles [6,20] reported partially on the same group of patients with skeletal anchorage. We did contact the authors of these articles for more information but did not get any response. Assuming that this was the same group of patients this leads to a total of 149 patients treated by conventional facemask-therapy and 125 patients treated with skeletal anchorage.

Inclusion and exclusion criteria of the included articles are summarized in Table 3.4. Only one article mentioned a sample size calculation [38]

Baseline comparability between treatment groups

No major baseline differences were described in 6 studies [6,17,19,20,38,40]. It was unclear whether major baseline differences existed in 2 studies [35,37]. Two studies compared three groups, two of which were treated and one untreated control group [19,37]

Characteristics of the intervention

Two studies evaluated the efficacy of facemask treatment with miniplates anchored to the upper jaw: Lee et al (2012)[17] evaluated the effect of facemask therapy with plates located in the upper jaw at the zygomatic buttress, Sar et al (2011)[19] placed the miniplates on the lateral nasal wall in the upper jaw. 3 articles [6,20,38] evaluated the use of 4 miniplates: 2 in the upper jaw positioned at the zygomatic buttress and 2 at the symphyseal area in the lower jaw. One article evaluated the use of miniscrews [35] in both jaws, one article evaluated the use of miniscrews on the palate in combination with a facemask [37] and one article reported on the use of miniscrews on the zygomatic buttress with a facemask [40]. All articles used conventional facemask treatment as control group, of which 7 with Rapid

Maxillary Expansion (RME) [6,17,19,20,35,37,40]. The conventional facemask group had a force of 300 to 800 g per side with a force vector of 15 to 30 degrees downward to the occlusal plane and were advised to wear the mask 12 to 16 hours per day.

Bone anchor systems

7 Different systems were included in this review:

Bollard anchors, tita-Link ®, Brussels Belgium [6,20]
Osteomed, Addison®, Tx, USA [19]
LeForte system, Jeil Medical ®, Seoul, Korea [17]
Benefit micro-implants, PSM Medical Solutions ®, Tutlingen, Germany [37]
Titanium miniplates, Trimed, titanium self-tapping screw ®, Ankara, Turkey[38]
Titanium miniscrew, Jeil Medical corp ®, Seoul Korea [35]
Miniscrew implants, ShenGang ®, ZhangHua, Taiwan [40]

Characteristics of outcome measures (For summary see also Table 3.6)

One article reported outcome measures by 3-dimensional analysis [20]. All other articles reported outcome measures by 2-dimensional conventional cephalometric analysis [6,17,19,35,37,38,40]. The reported outcome measures can be divided into 4 main categories: (1) skeletal effects, (2) dental effects, (3) vertical effects, and (5) soft tissue effects. Table 3.6 summarizes the reported outcome measures for each article.

Duration of follow-up

The included articles only reported a short follow up time ranging from 9.1 [38] to 14.4 [20] months in the skeletal anchorage treatment and from 6.2[38] to 13.2 [17] months in the conventional treatment group. One of the articles did not report any follow-up time [37]

Risk of bias in included studies (See summary Table 3.3)

Sequence generation

No studies reported an adequate sequence generation. Three articles [6,20,37] reported the results of 2 independent groups of consecutively treated patients and two articles [17,35] reported the results of a retrospective study. Also a high risk of selection bias was found in 2 articles because they used skeletal anchorage depending on patients' treatment preferences [38] or on patients' characteristics (subjects without anchorage teeth)[19]. One article was considered as having an unclear risk [40]

Allocation concealment

Allocation concealment was considered low in one study [40] and high in all other reported studies. Three articles [6,20,37] reported the results of 2 independent groups of consecutively treated patients and two articles [17,35] reported the results of a retrospective study. The two other studies also were considered as a high risk of allocation concealment because patients' characteristics [19] or treatment preferences [38] were used to allocate them to the skeletal anchorage group.

Blinding

Blinding of operators and trial participants was not possible in the included trials, which introduces the potential risk of performance bias in all studies. However blinding of outcome assessment (detection bias) was possible and is adequately performed and reported in one article [37]. In all other articles, it was unclear and only one author did reply that there was no blinding of the outcome assessment [40].

Selective reporting

Due to the nature of 5 of the studies (case control studies) included in this systematic review, they were judged to be at high risk of reporting bias [6,17,20,35,37]. The other three studies were judged to be at low [19,40] or unclear risk [38] of reporting bias.

Other potential sources of bias

Additional sources of bias were identified in one study [6]. In the latter study, two groups were compared by cephalometric analysis. In one group (face-mask treatment) data were collected by conventional radiograph and in the other group (bone-anchor treatment) lateral cephalograms were constructed out of Cone beam CT images, which may not give the same measurements as conventional radiographs. The remaining articles were not at risk of additional bias.

The overall risk of bias is summarized in Table 3.3. Overall, according to this study's evaluation, all studies were at high risk of bias.

In total 8 articles were included in this review, of which most of them were case control studies. Only three studies were conducted prospectively and all of them report only on a short follow-up time. All studies used conventional face-mask treatment as a control-group. Based on the type of anchorage, the studies could be divided into 3 groups.

1. facemask treatment anchored to the upper jaw with skeletal anchorage (4 articles [17,19,37,40]): There was sufficient evidence to determine a difference in skeletal sagittal effect when bone anchors were used. However, there was lack of evidence when miniscrews were used. All articles presented less dento-alveolar effects.

2. bone anchored maxillary protraction: anchors in upper and in lower jaw (3 articles [6,20,38]): There was sufficient evidence to determine a difference in skeletal sagittal effect and less dento-alveolar effect when bone anchors and / or miniscrews were used. Only when bone anchors were used in upper and lower jaw, there was significant less vertical change (autorotation of the mandible).

3. maxillary protraction by miniscrews in upper and lower jaw (1 article [35]): There was insufficient evidence to determine a difference in skeletal sagittal and vertical effect. On dento-alveolar changes, the position of the lower incisors was the only significant difference

Table 3.3: Risk of bias summary

	Random sequence generation (selection	Allocation concealment (selection bias)	Blinding of outcome assessment (detection	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Aglarci et al (2016)[38]	-	-	?	-	+	+
Cevidanes et al (2010)[6]	-	-	-	?	+	-
Ge et al (2012)[40]	?	+	-	+	+	+
Hino et al (2013)[20]	-	-	+	+	+	+
Jamilian et al (2011)[35]	-	-	?	-	+	+
Lee et al (2012)[17]	-	-	?	-	-	+
Ngan et al (2015)[37]	-	-	+	+	+	+
Sar et al (2011)[19]	-	-	?	?	+	+

+	low risk of bias
?	unclear risk of bias
-	High risk of bias

Table 3.4: Inclusion and exlusion criteria

Table 3.4 Inclusion and exclusion criteria														
Author (year)	Inclusion criteria							Exclusion criteria						
	dental		skeletal			Vertical growth pattern mandible	Prepubertal stage of skeletal maturity	Cleft syndrome	Previous orthodontic treatment	Previous surgical intervention	Skeletal asymmetry	Functional class III	Failure implant (>1)	Medical compromised patient
	Ant crossbite	Molar class III	ANB	Witts'	A – N perp									
Aglarci et al (2016)[38]	✓		≤0	≤-1		✓	✓	✓	✓			✓	✓	
Cevidanes et al (2010)[6]	✓	✓		≤-1										
Ge et al (2012) [40]	✓		≤0	≤-2			✓	✓			✓			✓
Hino et al (2013)[20]	✓	✓		≤-1										
Jamilian et al (2011)[35]		✓	≤0			✓		✓	✓	✓	✓			✓
Lee et al (2012) [17]	✓		≤-1		≤0		✓	✓			✓			
Ngan et al (2015)[37]	✓	✓	≤-2	≤-3				✓	✓					
Sar et al (2011)[19]	✓			≤-2	≤1	✓								

Table 3.5: Study characteristics

Table 3.5 study characteristics												
	Subjects								Methodology			
Author (year)	Testing group				Control group				Prospective	Randomisation	Follow-up time (T / C)	Analysis
	Nº	Mean age (yrs) (range)	technique	anchorage	Nº	Mean age (yrs) (range)	technique	anchorage				
Aglarci et al (2016)[38]	25	11,75 (1,23)	BAMP	Screw / Anchor	25	11,21 (1,32)	FM	FM / Hyrax	✓	✓	9,12 / 6,24	2D
Cevidanes et al (2010)[6]	21	11,8 (1,8)	BAMP	Anchor/ Anchor	34	8,25 (1,8)	FM/ RME	FM / Hyrax	✗	✗	6,78 / 9,45	2D/ Hybrid
Ge et al (2012) [40]	20	10,3	FM / MSI	Screw/ FM	23	10,5	FM/ RME	FM / Hyrax	✓	✓	11,0 / 13,0	2D
Hino et al (2013)[20]	25	11,9 (1,8)	BAMP	Anchor/ Anchor	21	8,1 (1,5)	FM/ RME	FM / Hyrax	✗	✗	14,4 / 10,1	3D
Jamilian et al (2011)[35]	10	10,5 (1,5)	MSI/ MSI	Screw / Screw	10	11,3 (0,8)	FM/ RME	FM / Hyrax	✗	✗	11,0 / 13,0	2D
Lee et al (2012)[17]	10	11,2 (1,2)	FM / Anchor	Anchor / FM	10	10,7 (1,3)	FM / RME	FM / Hyrax	✗	✗	12,0 / 13,2	2D
Ngan et al (2015)[37]	20	9,6 (1,2)	FM / HH	HH / FM	20	9,8 (1,6)	FM/ RME	FM / Hyrax	✗	✗	?	2D
Sar et al (2011)[19]	15	10,91	FM / Anchor	Anchor/ FM	15	10,31	FM/ RME	FM / Hyrax	✓	✗	6,78 / 9,45	2D

Abbreviations:
S: Significant; NS: Non-Significant; D: Downward; B: Backward; E: Extrusion; M: Mesialisation; P: Protrusion; R: Retrusion
* Color coded surface distances would show greater dental compensations than skeletal compensations in the Face-mask group in 10 patients
Color code: Green: skeletal anchorage more effect; Red: dental anchorage more effect

DISCUSSION

The use of skeletal anchorage has gained popularity among orthodontists and surgeons, with no consensus regarding indications, techniques, age, protocols or forces employed. It gained popularity because of potential advantages and possible better patient compliance. Patient compliance could be higher with these techniques as some of them rely only on intraoral elastics and not on extra-oral devices which are bulkier. It is also proposed that a favorable maxillary response can be obtained with moderate continuous traction rather than heavy interrupted forces during the day [42]. However widely used, skeletal anchorage procedures do come with possible drawbacks: it involves more or less invasive procedures to place and subsequently remove the devices. Also some of types are not stable throughout treatment [10,43]. Only one systematic review with meta-analysis was published evaluating the effect of skeletal anchorage in general in interceptive treatment of class III malocclusion [44]. Half of the studies included in this review had a positive control group and the other half did compare the effects with an untreated group. This review concluded that there was no evidence that treatment with skeletal anchorage produces more (or faster) skeletal effect then conventional treatment. This review also stated that there is a lack of randomized controlled trials and a lack of standardization, which does not favor meta-analysis.

This systematic review showed insufficient evidence regarding the effects of skeletal anchorage in interceptive class III treatment to support definitive conclusions on long term skeletal effects and stability. Only 8 studies were included and most of them were case control studies with short follow-up time (range from 6.8 to 14.4 months). It should not be forgotten that the 8 articles included are the result of a very exacting selection process. Many articles published as clinical cases or case series have not been included but could also provide valuable information for subsequent studies of higher evidence quality.

In the short term it seems that bone-anchors can provide more skeletal effect with less dento-alveolar compensations and less unwanted vertical changes. This does not always exclude the use of a facemask. The use of miniscrews as skeletal anchorage device does not seem to provide more skeletal effect, although it could minimize the unwanted dental effects in the upper jaw.

There is a need for more well-designed randomized controlled trials to support the conclusions of the current literature. It is also suggested that those trials focus on long term clinical outcome parameters such as skeletal effect (and stability) and the need for orthognathic surgery. Also, attention should be given to aesthetic results and patient satisfaction in order to evaluate the possible benefits of the additional effect acquired by using skeletal anchorage.

Addendum

A 2020 systematic review and meta-analysis [45] comparing Bone Anchored Maxillary Protraction (BAMP) to controls confirmed our 2018 findings. While BAMP with Facemask (BAFM) showed statistically significant improvements in ANB angle compared to traditional Facemask therapy, these differences were not clinically meaningful. No significant differences were found in Wits appraisal. The authors emphasized that evidence supporting maxillary advancement through BAMP was of low quality, citing poor study designs and reliance on historical control groups. Therefore, the clinical advantages of BAMP over traditional facemask therapy remain uncertain. Caution should be made as this systematic review also included retrospective studies.

A 2022 systematic review and network meta-analysis [46] comparing different types of bone anchored maxillary protraction did yield somewhat different conclusions. Skeletal changes: Bone-anchored maxillary protraction devices promoted greater forward movement of the maxilla and better correction of Class III intermaxillary relationships compared to tooth-anchored devices. Bone-anchored facemask (BAFM) caused the greatest advancement of the A point, while bone-anchored intermaxillary protraction (BAIP) had the best effect in improving ANB and Wits measurements.

1. Mandibular growth: All maxillary protraction techniques inhibited sagittal mandibular growth in the short term, but there were no significant differences between anchorage types.

2. Vertical changes: Bone-anchored groups showed significantly less mandibular rotation and lower face height increase compared to other groups.
3. Dental changes: Bone-anchored devices significantly reduced labial proclination of maxillary incisors compared to tooth-anchored devices. Groups using facemasks showed lingual inclination of lower incisors, while those using intermaxillary elastics showed labial proclination.
4. Treatment effects: BAIP yielded the best overall treatment effect among the interventions studied. It provided greater skeletal effects (over 90%) in correcting overjet compared to other techniques.

Caution should be made as this systematic review also included Controlled Clinical Trials (CCT) where BAMP was compared with control groups.

The inclusion of CCT and retrospective analyses is driven by the scarcity of high-quality RCTs comparing the outcomes of dental and bone anchored solutions. This limitation could introduce potential bias, potentially impacting the results and conclusions of both systematic reviews.

REFERENCES

1. De Toffol, L., Pavoni, C., Baccetti, T., Franchi, L. & Cozza, P. Orthopedic Treatment Outcomes in Class III Malocclusion. *Angle Orthodontist* **78**, (2008).
2. Rongo, R. *et al.* Skeletal and dental effects of Class III orthopaedic treatment: a systematic review and meta-analysis. *J Oral Rehabil* (2017) doi:10.1111/joor.12495.
3. Woon, S. C. & Thiruvenkatachari, B. Early orthodontic treatment for Class III malocclusion: A systematic review and meta-analysis. *Am J Orthod Dentofacial Orthop* **151**, 28–52 (2017).
4. Ellis III, E. & McNamara Jr., J. A. Components of adult class III malocclusion. *Journal of Oral and Maxillofacial Surgery* **42**, 295–305 (1984).
5. De Clerck, H. J. & Proffit, W. R. Growth modification of the face: A current perspective with emphasis on Class III treatment. *American Journal of Orthodontics and Dentofacial Orthopedics* Preprint at https://doi.org/10.1016/j.ajodo.2015.04.017 (2015).
6. Cevidanes, L., Baccetti, T., Franchi, L., McNamara, J. A. & De Clerck, H. Comparison of two protocols for maxillary protraction: bone anchors versus face mask with rapid maxillary expansion. *Angle Orthod* **80**, 799–806 (2010).
7. Nienkemper, M., Wilmes, B., Franchi, L. & Drescher, D. Effectiveness of maxillary protraction using a hybrid hyrax-facemask combination: *A controlled clinical study*. *Angle Orthod* **85**, 764–770 (2015).
8. Rodríguez de Guzmán-Barrera, J. *et al.* Effectiveness of interceptive treatment of class III malocclusions with skeletal anchorage: A systematic review and meta-analysis. *PLoS One* **12**, e0173875 (2017).
9. Wilmes, B. *et al.* The Hybrid Hyrax Distalizer, a new all-in-one appliance for rapid palatal expansion, early class III treatment and upper molar distalization. *J Orthod* **41**, s47–s53 (2014).
10. Bozkaya, E., Yuksel, A. S. & Bozkaya, S. Zygomatic miniplates for skeletal anchorage in orthopedic correction of class III malocclusion: A controlled clinical trial. *Korean J Orthod* **47**, 118–129 (2017).
11. Şar, Ç., Şahinoğlu, Z., Özçirpici, A. A. & Uçkan, S. Dentofacial effects of skeletal anchored treatment modalities for the correction of maxillary retrognathia. *American Journal of Orthodontics and Dentofacial Orthopedics* **145**, (2014).
12. Enacar, A., Giray, B., Pehlivanoglu, M. & Iplikcioglu, H. Facemask therapy with rigid anchorage in a patient with maxillary hypoplasia and severe oligodontia. *Am J Orthod Dentofacial Orthop* **123**, 571–7 (2003).
13. Hong, H., Ngan, P., Han, G. L., Liu, G. Q. & Wei, S. H. Y. Use of onplants as stable anchorage for facemask treatment: A case report. *Angle Orthodontist* **75**, 453–460 (2005).
14. Jamilian, A. & Showkatbakhsh, R. Treatment of maxillary deficiency by miniscrew implants--a case report. *J Orthod* **37**, 56–61 (2010).
15. Kaya, D., Kocadereli, I., Kan, B. & Tasar, F. Effects of facemask treatment anchored with miniplates after alternate rapid maxillary expansions and constrictions; a pilot study. *Angle Orthod* **81**, 639–646 (2011).
16. Kircelli, B. H., Pektaş, Z. O. & Uçkan, S. Orthopedic protraction with skeletal anchorage in a patient with maxillary hypoplasia and hypodontia. *Angle Orthodontist* **76**, 156–163 (2006).

17. Lee, N.-K., Yang, I.-H. & Baek, S.-H. The short-term treatment effects of face mask therapy in Class III patients based on the anchorage device: miniplates vs rapid maxillary expansion. *Angle Orthod* **82**, 846–52 (2012).
18. Baek, S.-H., Kim, K.-W. & Choi, J.-Y. New treatment modality for maxillary hypoplasia in cleft patients. Protraction facemask with miniplate anchorage. *Angle Orthod* **80**, 783–91 (2010).
19. Sar, C., Arman-Ozcirpici, A., Uckan, S. & Yazici, A. C. Comparative evaluation of maxillary protraction with or without skeletal anchorage. *Am J Orthod Dentofacial Orthop* **139**, 636–649 (2011).
20. Hino, C. T. *et al.* Three-dimensional analysis of maxillary changes associated with facemask and rapid maxillary expansion compared with bone anchored maxillary protraction. *American Journal of Orthodontics and Dentofacial Orthopedics* **144**, 705–714 (2013).
21. Elnagar, M. H., Elshourbagy, E., Ghobashy, S., Khedr, M. & Evans, C. A. Comparative evaluation of 2 skeletally anchored maxillary protraction protocols. *Am J Orthod Dentofacial Orthop* **150**, 751–762 (2016).
22. De Clerck, H., Cevidanes, L. & Baccetti, T. Dentofacial effects of bone-anchored maxillary protraction: A controlled study of consecutively treated Class III patients. *American Journal of Orthodontics and Dentofacial Orthopedics* (2010) doi:10.1016/j.ajodo.2009.10.037.
23. Zhang, W., Qu, H. C., Yu, M. & Zhang, Y. The effects of maxillary protraction with or without rapid maxillary expansion and age factors in treating Class III malocclusion: A meta-Analysis. *PLoS One* (2015) doi:10.1371/journal.pone.0130096.
24. Ngan, P. *et al.* Cephalometric and occlusal changes following maxillary expansion and protraction. *Eur J Orthod* **20**, 237–254 (1998).
25. Nartallo-Turley, P. E. & Turley, P. K. Cephalometric effects of combined palatal expansion and facemask therapy on Class III malocclusion. *Angle Orthod* **68**, 217–224 (1998).
26. Vaughn, G. A., Mason, B., Moon, H.-B. & Turley, P. K. The effects of maxillary protraction therapy with or without rapid palatal expansion: a prospective, randomized clinical trial. *Am J Orthod Dentofacial Orthop* **128**, 299–309 (2005).
27. Macdonald, K. E., Kapust, A. J. & Turley, P. K. Cephalometric changes after the correction of class III malocclusion with maxillary expansion/facemask therapy. *Am J Orthod Dentofacial Orthop* **116**, 13–24 (1999).
28. Iwasaki, H., Ishikawa, H., Chowdhury, L., Nakamura, S. & Iida, J. Properties of the ANB angle and the Wits appraisal in the skeletal estimation of Angle's Class III patients. *Eur J Orthod* **24**, 477–483 (2002).
29. Jarvinen, S. An analysis of the variation of the ANB angle: a statistical appraisal. *Am J Orthod* **87**, 144–146 (1985).
30. Sadat-Khonsari, R. *et al.* Geometric influence of the sagittal and vertical apical base relationship on the ANB angle. *J Orofac Orthop* **70**, 152–158 (2009).
31. Adams, G. L., Gansky, S. A., Miller, A. J., Harrell, W. E. J. & Hatcher, D. C. Comparison between traditional 2-dimensional cephalometry and a 3-dimensional approach on human dry skulls. *Am J Orthod Dentofacial Orthop* **126**, 397–409 (2004).
32. Cevidanes, L. H. C., Heymann, G., Cornelis, M. A., DeClerck, H. J. & Tulloch, J. F. C. Superimposition of 3-dimensional cone-beam computed tomography models of growing patients. *Am J Orthod Dentofacial Orthop* **136**, 94–99 (2009).

33. Liberati, A. *et al.* & reporting The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions : explanation and elaboration. (2009) doi:10.1136/bmj.b2700.
34. Higgins JPT, Altman DG, S. J. (Editors). Chapter 8: Assessing risk of bias in included studies. in *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011).* (2011). doi:10.1001/jama.2013.109501.Conflict.
35. Jamilian, A., Haraji, A., Showkatbakhsh, R. & Valaee, N. The effects of miniscrew with Class III traction in growing patients with maxillary deficiency. *Int J Orthod Milwaukee* **22**, 25–30 (2011).
36. Kircelli, B. H. & Pektas, Z. Ö. Midfacial protraction with skeletally anchored face mask therapy: A novel approach and preliminary results. *American Journal of Orthodontics and Dentofacial Orthopedics* **133**, 440–449 (2008).
37. Ngan, P. *et al.* Comparison of two maxillary protraction protocols: tooth-borne versus bone-anchored protraction facemask treatment. *Prog Orthod* **16**, (2015).
38. Ağlarcı, C., Esenlik, E. & Fındık, Y. Comparison of short-term effects between face mask and skeletal anchorage therapy with intermaxillary elastics in patients with maxillary retrognathia. *Eur J Orthod* **38**, 313–23 (2016).
39. Coscia, G., Addabbo, F., Peluso, V. & D'Ambrosio, E. Use of intermaxillary forces in early treatment of maxillary deficient class III patients: results of a case series. *J Craniomaxillofac Surg* **40**, e350-4 (2012).
40. Ge, Y. S., Liu, J., Chen, L., Han, J. L. & Guo, X. Dentofacial effects of two facemask therapies for maxillary protraction Miniscrew implants versus rapid maxillary expanders. *Angle Orthodontist* **82**, 1083–1091 (2012).
41. Ge, Y. S., Liu, J., Chen, L., Han, J. L. & Guo, X. Dentofacial effects of two facemask therapies for maxillary protraction Miniscrew implants versus rapid maxillary expanders. *Angle Orthodontist* **82**, 1083–1091 (2012).
42. De Clerck, H. J., Cornelis, M. A., Cevidanes, L. H., Heymann, G. C. & Tulloch, C. J. F. Orthopedic traction of the maxilla with miniplates: a new perspective for treatment of midface deficiency. *J Oral Maxillofac Surg* **67**, 2123–2129 (2009).
43. De Clerck, E. E. B. & Swennen, G. R. J. Success rate of miniplate anchorage for bone anchored maxillary protraction. *Angle Orthodontist* **81**, 1010–1013 (2011).
44. Rodríguez de Guzmán-Barrera, J. *et al.* Effectiveness of interceptive treatment of class III malocclusions with skeletal anchorage: A systematic review and meta-analysis. *PLoS One* **12**, e0173875 (2017).
45. Cornelis, M. A., Tepedino, M., Riis, N. de V., Niu, X. & Cattaneo, P. M. Treatment effect of bone-anchored maxillary protraction in growing patients compared to controls: a systematic review with meta-analysis. *Eur J Orthod* 1–18 (2020) doi:10.1093/ejo/cjaa016.
46. Wang, J. *et al.* Clinical effectiveness of different types of bone-anchored maxillary protraction devices for skeletal Class III malocclusion: Systematic review and network meta-analysis. *Korean J Orthod* **52**, 313–323 (2022).

CHAPTER 4

Bone anchor efficacy in routine clinical practice

This chapter is based on the following manuscript.

Van Hevele J, Nout E, Claeys T, Meyns J, Scheerlinck J, Politis C.
Bone-anchored maxillary protraction to correct a class III skeletal relationship: multicenter retrospective analysis of 218 patients. *Journal of cranio-maxillofacial Surgery 2018; 46: 1800-1806.*

ABSTRACT

This study evaluated the impact of class III correction by elastic traction on four miniplates and the failure rate of bone-anchored miniplates in non-syndromic patients. A total of 218 patients (112 males and 106 females; average 11.4 years) treated by 38 orthodontists, received four miniplates (total 872 miniplates) from 2008 to 2016 at three maxillofacial centers in two countries. Factors affecting the success and failure of the miniplates were retrospectively examined and skeletal changes on cephalometric radiographs examined for 52 patients. Elastic traction was performed for 22.9 months on average. The miniplate survival rate was 93.6%; 25.7% of the patients suffered failure of one of the miniplates. Postoperative antibiotics and placement of the neck of the miniplate in the attached gingiva significantly improved the success rate. Miniplate failure was 6-times higher in the maxilla and occurred more in younger patients. Self-drilling screws were significantly better than self-tapping screws to fix the miniplate. Small cephalometric changes were seen: SNA (+ 1.9°), SNB (+0.4°), ANB (+1.4°), Wits analysis (+1.3 mm). In conclusion, bone-anchored maxillary protraction on four miniplates is an effective method for correcting a class III relationship but has less skeletal effect than previously reported in the literature.

INTRODUCTION

The incidence of class III malocclusion is relatively low (5-6%) in Caucasian patients and relatively high (9 - 22.4%) in the Asian population[1–5] . A class III skeletal deformity may be caused by a hypoplastic maxilla, prognathic mandible, or a combination of both. In Asians, 47.7% of class III deformities are due to mandibular prognathism, whereas in the Caucasian population a hypoplastic upper jaw is the main cause of a skeletal class III deformity [6,7] .

Untreated class III patients have horizontal forward growth of the symphysis of the mandible and a tendency for upward and backward growth of the condyle combined with mild horizontal backward deformation of the maxillary region (maxillary retrusion with growth). These characteristics show a lack of self-improvement of the facial skeleton in untreated class III patients and suggest a rationale for class III treatment by stimulating anterior growth of the maxilla and preventing anterior growth of the mandible [8].

In the past, many different orthopedic appliances have been used for maxillary protraction to treat children with maxillary deficiency, such as Frankel's bionator, reverse twin-block, FR-3 appliances as well as removable mandibular retractor, and double-piece correctors [5,9,10]. Regrettably, many retrospective studies have shown that functional appliances have little to no skeletal effect [11]. In cases of a prognathic mandible, chin cup treatment for 7-12 hours a day has been developed to prevent growth of the mandible [12]. This technique also fails to exert a clear orthopedic effect - reduced prominence of the chin is due to backward and downward rotation of the mandible[11,13]. A more successful treatment option to achieve orthopedic changes is protraction of the maxilla using a Delaire facemask[14]. The biggest disadvantage of this tooth-borne technique is that an extraoral appliance has to be applied for at least 14-16 hours a day over 9-12 months to be effective[15]. There is no statistical difference in protraction when the patients have simultaneous expansion of the maxilla, but there is less dental compensation [16]. In general, tooth-borne facemask protraction results in counterclockwise rotation of the maxilla because the posterior part moves more downwards than the anterior part of the maxilla due to dentoalveolar compensation with extrusion and mesialization of the maxillary molars[11,16]. Other dentoalveolar changes are proclination and extrusion of the maxillary incisors and retrusion of the mandibular incisors. Facemask treatment with a chin cup is not only an effective method for maxillary advancement, but also inhibits mandibular growth and movement of point B. An undesired effect is posterior or clockwise rotation of the mandible[16–18].

Bone anchorage techniques have been developed to facilitate skeletal maxillary advancement and avoid dentoalveolar compensation. Facemask traction was applied on ankylotic maxillary canines, osseointegrated implants, titanium screws, onplants, or miniplates bilaterally on the apertura piriformis or zygomatic crest[18–24]. The use of paranasal skeletal anchorage with facemask already demonstrates significantly less counterclockwise rotation of the maxilla than tooth-born facemask treatment and less clockwise rotation of the mandible [25]. Instead, a systematic review and meta-analysis has shown approximately 30° downward and forward movement of the maxilla by facemask protraction on miniplates in the maxilla [5,26].

A critical factor in exerting orthopedic traction on the maxilla and/or mandible is the relatively strict age limit. The main goal of early intervention is to stimulate bone apposition at the open circummaxillary and circumzygomatic sutures [16,27–30]. The optimal treatment age is at the beginning of the first changing phase of the teeth (< 10 years), as starting treatment at a later age achieves less protraction and change in the maxillomandibular relationship with surgical intervention likely to be needed eventually[16].

In 2009, De Clerck et al.[31] presented a new technique called bone-anchored maxillary protraction (BAMP), in which intraoral elastics were fixed to four intraoral miniplates, eliminating dentoalveolar effects and facilitating patient compliance [8]. Other advantages include the non-interference of miniscrews with tooth movements and attachment unit of the miniplate close to the dental arch, which is an advantage when other orthodontic treatment is to be applied to the miniplates[32]. The biggest disadvantage is the need for invasive surgery to place the miniplates and remove the miniplates again after treatment [31,33]. The biggest disadvantages are postoperative inflammation, possible irritation of the adjacent tissues by the miniplates or elastics, and loosening of the miniplates because of a lack of bone quality at an early age [34] . Less patient compliance is needed than with the facemask, as the patient is only asked to change elastics daily, but it requires an additional effort in dental hygiene.

Some two-dimensional cephalometric studies and three-dimensional studies have been performed to analyze the skeletal changes in bone-anchored maxillary protraction with four intraoral miniplates[35]. A recent systematic review and meta-analysis compared class III elastic traction on miniplates with facemask and control groups by examining the change in SNA, SNB, ANB, overjet, and Wits [4]. All of these studies used a small number of patients in proving the success rate of the miniplates and rate of skeletal correction. Therefore, we wanted to examine both important parameters in a larger population of patients referred for class III elastic traction on miniplates, including those with a small class III skeletal relationship.

MATERIAL AND METHODS

This retrospective multicenter study was performed from 2010 to 2016 in two departments of oral and maxillofacial surgery in Belgium and one department of oral and maxillofacial surgery in the Netherlands. This study was approved by the Medical and Ethical Committee in both countries (NW2016-62).

Patients who were referred by their orthodontist for four miniplates for class III elastic traction were included when pre-operative, postoperative data and radiological data (lateral X-ray and panoramic X-ray) were present in the medical records of the surgeons and/or orthodontists. Syndromic patients and cleft patients were excluded. In 218 patients (112 males and 106 females), 872 pediatric or adult Bollard bone anchors (Titalink ®, Belgium) were placed between 2010 and 2016 at the zygomatic buttresses in the maxilla and between the second incisors and canines in the lower jaw. A total of 127 patients were operated on in Belgium and 91 patients in the Netherlands. The mean age at the time of surgery was 11.4 years (range 9 – 14 years). The mean follow-up was 19.6 (SD 13.4) months. Amoxicillin clavulanic acid was administered preoperatively. In cases of allergy, clindamycin was given. In the two participating Belgian hospitals, De Clerck's technique was used in which the horizontal incision line of the L-shaped incision was 1 mm into the attached gingiva[36]. In these centers, a bone anchor with three fixation holes was used in the upper jaw; in the lower jaw, a bone anchor with two fixation holes was placed. In the participating Dutch hospital, this technique was modified as follows: the horizontal line was incised 1 mm below the mucogingival junction to allow proper stitching and maxillary bone anchors with three fixation holes were used in both the upper and lower jaw. At all participating centers, plates were fixed by self-tapping (pre-drilling with conical drill) or self-drilling fixation screws, 5 or 7 mm in length and 2.0 mm in diameter. Resorbable stitches were used in all patients.

Postoperatively, patients were instructed to use a chlorhexidine mouth rinse three times a day for 5 days. Analgesics and non-steroidal anti-inflammatory drugs were prescribed. Only Belgian patients received postoperative oral antibiotics for 5 days. After 10 to 14 days, the orthodontist started with elastic traction of 100 g and increased the force weekly until a maximum force of 250 g was reached on each side [35]. This is less than tooth-borne facemask orthopedic traction, in which 400 to

450 g is applied on each side [37]. Patients had to change the elastics on both sides daily. Postoperative controls were managed by the orthodontist at monthly intervals. Patients were referred to the oral and maxillofacial surgery for removal of the bone anchors, or in the case of infection or fracture.

All patients received a study number and all data collected anonymously in Data Management, Research Manager (Cloud9 Software). The following parameters were evaluated: surgical technique, gender, age at surgery, type of bollard bone anchor, type of fixations screw, reason for failure, quadrant of failure, time to failure, and total time of elastic traction. Loosening or fracture of a miniplate was scored as a failure.

Cephalometric analysis was performed by the first author using OnyxCeph OMS software (Image Instruments, Chemnitz, Germany). In 136 of 218 patients, the class III elastic treatment was finished by the end of this study. Both preoperative and post-elastic treatment lateral X-rays with measurement lines were only available for 52 patients. Therefore, SNA, SNB, ANB, and Wits analysis were performed in 52 cases. The error in locating, superimposing, and measuring the changes in the landmarks by one examiner was measured on the lateral X-rays of 10 randomly selected subjects. All lateral X-rays were recorded twice, independently, on two separate occasions, with a 2-week interval. For all the cephalometric variables, differences between the independent repeated measurements for each individual before/after treatment were recorded. The intraclass correlation coefficient of reliability (R) was used to determine the reliability of cephalometric measurements. The R value can range from 0 to 1.00, values greater than 0.90 indicating high reliability. The correlations for all the cephalometric variable ranges from 0.96 to 0.99, with most being above 0.98.

Statistical analyses were performed in SPSS Statistics (version 24, IBM) by a professional statistician. The success rates of different groups were compared in a general linear mixed model for binary responses using a logit link. A survival model using parametric regression, presuming a Gaussian distribution, was fit to the data to find the time to failure. To analyze cephalometric data, a student’s t-test was used to find differences between groups. Data were evaluated for a normal distribution around their own mean using a normal quantile plot. The Bartlett's test was applied to check the homogeneity of variance. A linear regression model was applied for continuous variables, such as starting age. Residuals were evaluated for their normality using a normal quantile plot.

RESULTS

During the study period, 872 miniplates were placed in 218 patients. The mean duration of elastic traction was 22.9 (SD 13.4) months. In 22 (10 %) patients, the elastic traction therapy was prematurely ended due to loss of the bone anchor or bad patient compliance. In 52 finishes cases, class III skeletal correction was measured by cephalometric analysis.

Complications

Several types of complications were observed. Fifty-six (25.7%) patients experienced failure of one of the miniplates, which required replacement. Of these patients, 37 experienced mobile miniplates and 11 had broken miniplates. Five patients required a new surgery to remove an infected miniplate and three patients to correct mucosal excess. One tooth (0.5%) became non-vital after drilling in the root of the lower canine, but the miniplate remained functional and was removed after finishing the class III treatment. In 51 of the 56 patients with a failed miniplate that required removal, we were able to determine the moment of failure during the treatment. In these patients, the mean time to failure was 9.4 months after placement (median 4.8 months; SD 12.5); the mean time to failure in Belgium was 8.8 months and in the Netherlands 9.7 months (Figure 4.1).

Center

We found a significant difference ($p < 0.01$) between the failure rate in the Netherlands and Belgium. In the Netherlands, 36 (39.6%) of the 91 patients encountered a failure of a bone anchor, whereas in Belgium, 20 (15.7%) of the 127 patients presented with a failure. Regarding miniplates, 328 (90%) of 364 miniplates survived in the Netherlands and 488 (96%) of 508 survived in Belgium, giving an overall success rate of 93.6% (816 of the 872 miniplates; Table 4.1).

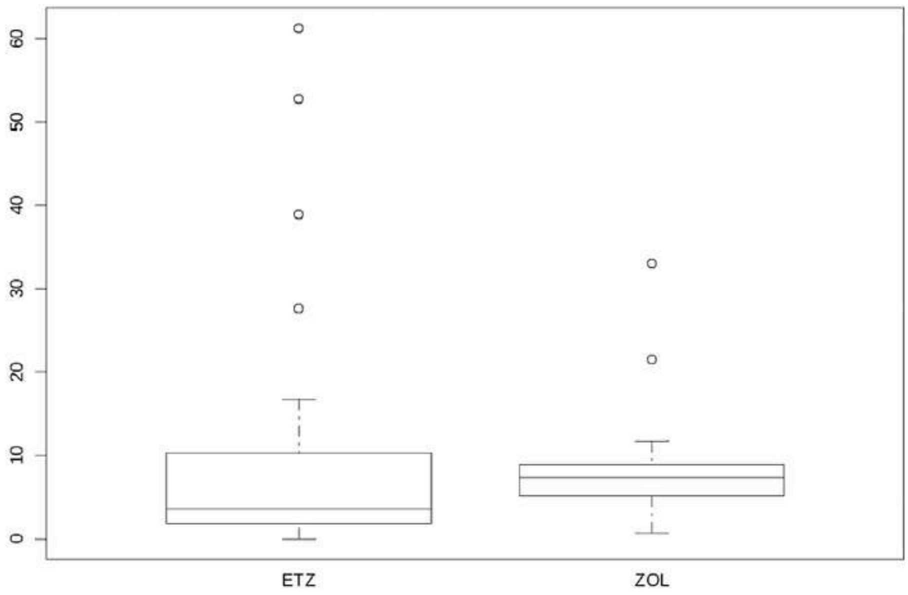


Figure 4.1. Time to failure is 9.7 months (y-axis) in the Netherlands (ETZ) and 8.8 months in the Belgian centers.

Table 4.1: Success rate of class III miniplates in Belgium (BE) and the Netherlands (NL) for all included patients. Differences in the success rate for patients and miniplates are shown.

Survival	Patients NL	Patients BE	Patients total	Miniplates NL	Miniplates BE	Miniplates total
Total number	91	127	218	364	508	872
Successful, n (%)	55 (60.4%)	107 (84.3%)	162 (74.3%)	328 (90%)	488 (96%)	816 (93.6%)

Maxilla/mandible

Miniplate failure was six times higher in the upper jaw than in the lower jaw; 48 (85.7%) patients experienced a failure in the maxilla and eight patients (14.3%) experienced a failure in the mandible. Forty-eight of the 436 zygomatic bone anchors failed, giving a success rate of 89.0% for all bone anchors placed in the upper jaw. In the lower jaw, the success rate for all placed bone anchors was 98.2%. The mean time interval between the start of treatment and miniplate failure was 8.5 months in the upper jaw and 15.2 months in the lower jaw.

Age

More failures occurred at a younger age in boys, but not in girls (Figure 4.2). To compare the failure rate according to age, we divided the population into two groups, using 11 years old as the threshold. In the literature, the ideal age for placing intraoral miniplate traction is 10 and 12 years old. No significant difference was found between the age groups or between boys and girls when considering miniplate failure. Table 4.2 provides an overview of gender and age.

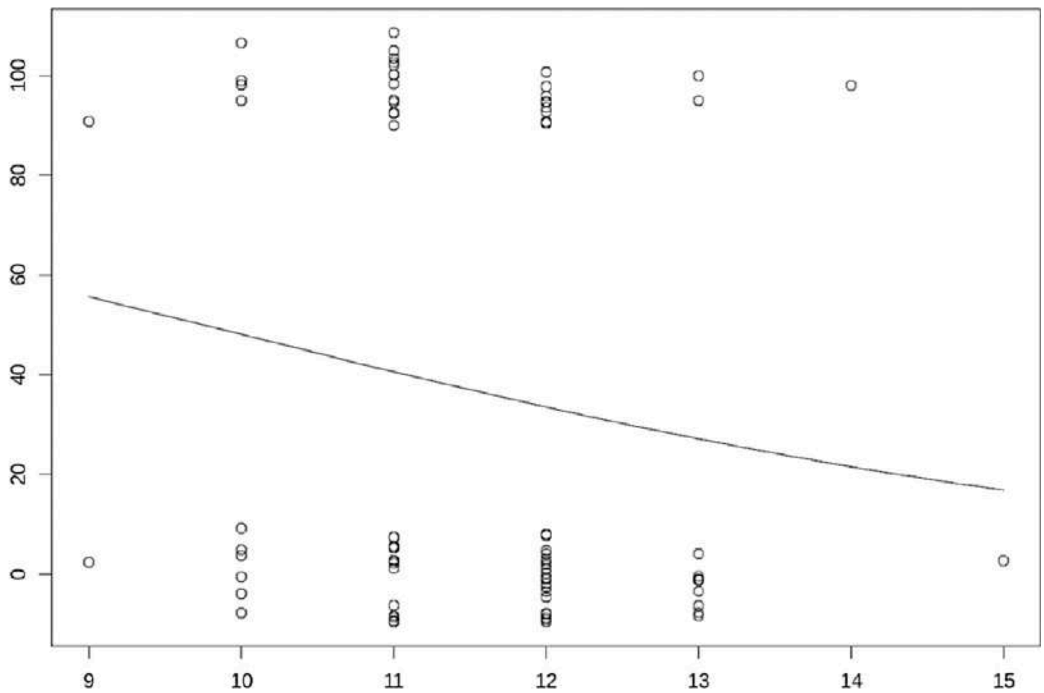


Figure 4.2. Chance of failure (% on y-axis) in 81 boys who completed class III treatment based on the starting age (x-axis) of treatment.

Table 4.2: Success and failure rates for all patients based on starting age and gender.

	Boys > 11yrs	Boys < 11yrs	Girls >11 yrs	Girls <11 yrs	All patients > 11 yrs	All patients < 11 yrs	Total patients
Success, n (%)	47 (79.7%)	35 (64.8%)	28 (77.8%)	52 (75.4%)	75 (78.9%)	87 (70.7%)	162 (74.3%)
Failure, n (%)	12 (20.3%)	19 (35.2%)	8 (22.2%)	17 (24.6%)	20 (21.1%)	36 (29.3%)	56 (25.7%)
No. of patients	59	54	36	69	95	123	218

Type of screw

Among the 218 patients, 96 received self-drilling screws and 122 received self-tapping screws. Failure occurred in 9 (9.4%) patients with self-drilling screws and 47 (38.5%) patients with self-tapping screws ($p = 0.00$; Table 4.3).

Table 4.3: Success and failure rates in patients based on self-drilling and self-tapping screws.

	Self-drilling	Self-tapping	Total patients
Success, n (%)	87 (90.6%)	75 (61.5%)	162 (74.3%)
Failure, n (%)	9 (9.4%)	47 (38.5%)	56 (25.7%)
No. of patients	96	122	218

Radiographic analysis

Cephalometric analysis was performed in the 52 patients (29 males, 23 females) with lateral X-rays both before surgery (T1) and after finishing class III elastic traction (T2). The data for the total cohort are summarized in Table 4.4. The mean pre-operative (T1) SNA was similar in males (79.2°) and females (79.6°) and in both countries (79.7° in the Netherlands and 79.0° in Belgium). The cephalometric data after finishing class III elastic traction were still similar in males and females in both countries (SNA: males 81.4°, females 81.1°; the Netherlands 81.4°, Belgium 81.1°). This confirms the positive effect on the A-point. The mean difference between T2 and T1 for advancement of the A-point was 1.6 mm.

The mean pre-operative SNB was 80.1° in males and 81.0° in females, and 80.8° in the Netherlands and 80.3° in Belgium. The mean post-treatment SNB was 81.1° in males and 80.9° in females, and 81.6° in the Netherlands and 80.3° in Belgium. The data for SNA and SNB were confirmed by the mean change of +1.4° for ANB (Figure 4.3). The mean pre-operative ANB was -1.0° in males and -1.3° in females, and -1.0° in the Netherlands and -1.2° in Belgium. The mean post-treatment ANB was 0.3° in males and 0.4° in females, and -0.1° in the Netherlands and 0.9° in Belgium.

The mean pre-operative Wits analysis was -4.0 mm in males and -4.6 mm in females, and -3.9 mm in the Netherlands and -4.7 mm in Belgium. The mean post-treatment Wits analysis was -2.9 mm in males and -3.2 mm in females, and -3.5 mm in the Netherlands and -2.4 mm in Belgium, which gives a positive correction of the skeletal relationship (Figure 4.4 and Table 4.4). Comparing the ANB and Wits in patients < 11 years old and > 11 years old, we found a non-significant change in ANB of 1.54° (< 11 years) versus 1.12° (> 11 years) and no difference in the Wits analysis.

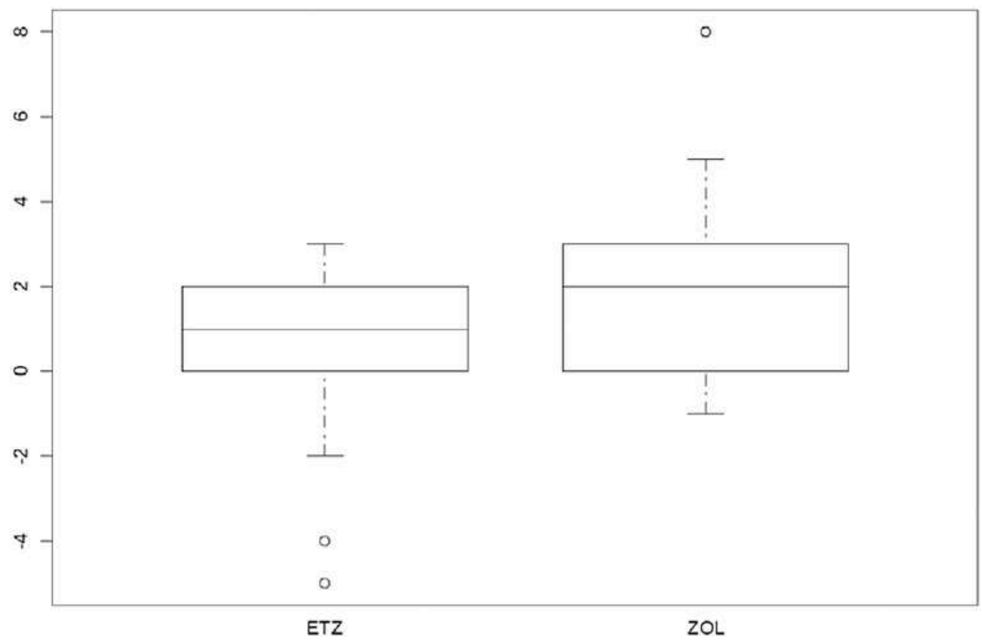


Figure 4.3. Distribution of correction of ANB (T2-T1) between the Netherlands (ETZ) and Belgium (ZOL)

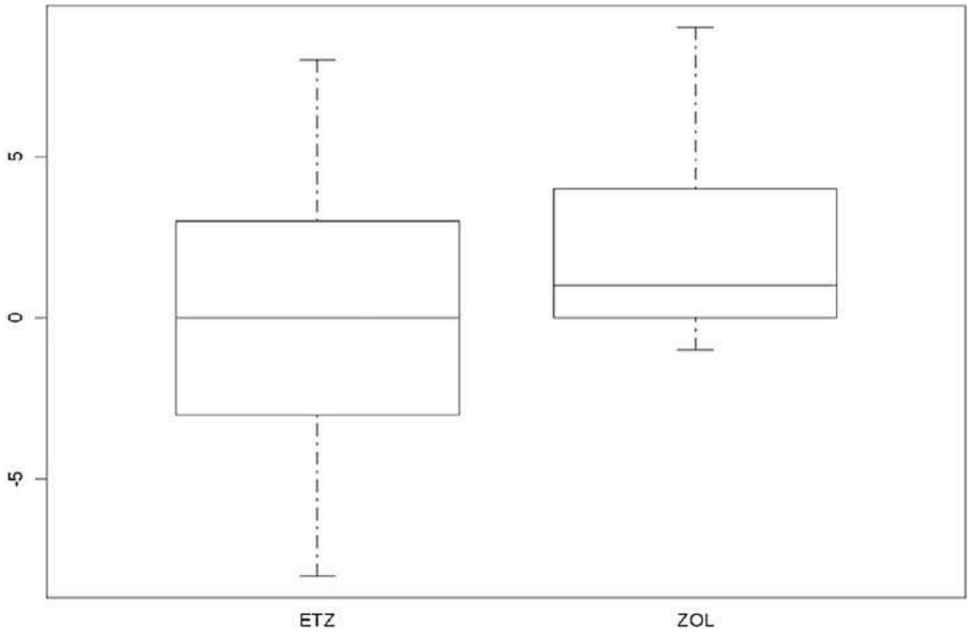


Figure 4.4. Distribution of correction of Wits analysis (T2-T1) between the Netherlands (ETZ) and Belgium (ZOL)

Table 4.4: Pre-operative (T1) and post-treatment (T2) cephalometric data and the differences in 52 finished cases with available pre-operative and post-treatment lateral X-rays.

	Pre-operative (T1)	Post-treatment (T2)	Difference (T2-T1)
SNA	79.4°	81.3°	+ 1.9°
SNB	80.6°	81.0°	+ 0.4°
ANB	-1.1°	0.3°	+ 1.4°
Wits	- 4.3 mm	- 3.0 mm	+ 1.3 mm

DISCUSSION

Bone-anchored maxillary protraction to treat class III skeletal deformities has gained popularity over treatment with a facemask. The greatest advantages are the possibility of 24-hour/day intraoral traction without an external facemask, requiring less patient compliance. However, the literature concerning class III correction with four miniplates is limited to a few case reports, case series, and recently a systematic review of intraoral skeletal class III elastic traction with four miniplates [4]. In general, treatment with bone anchors could have a greater skeletal effect in the short-term with less dentoalveolar compensation and possibly less autorotation of the lower jaw, with minimal miniplate failure. In this study, we included 218 patients from 38 orthodontists to obtain a good overview of the use of class III traction and compare successes and failures in an average population of patients and orthodontists. Ten percent of our patients were forced to stop the treatment before achieving good correction of the class III deformity. The main reasons for stopping treatment were loosening of the miniplates without replacing, not enough progression during treatment, and lack of cooperation by the patient.

The overall success rate of the miniplates was 93.6%, which is in line with the 92-99% reported in the literature [32,34,38]. There is no difference in literature for immediate loading or delayed loading after 2 months [39]. Unfortunately, the failure rate of bone anchors on the treatment level per patient is much higher. In the present study, 25.7% of patients had a failure of one of the miniplates, which is much higher than in previous studies. Mommaerts et al.[39] reported the failure of orthodontic bone anchors placed for various indications in 11.7% of their Belgian patients, which is in line with the 15.7% for Belgian patients in the present study, but the failure rate in patients from the Netherlands was significantly higher (39.6%). Analysis of both treatment protocols revealed only differences concerning the administration of postoperative antibiotics, which did not occur in the Netherlands, and different placement protocols, in which the neck of the bone anchor was placed under the gingival border into the loose mucosa in the Netherlands instead of 1 mm in the attached gingiva in Belgium. In this study, we cannot differentiate which parameter is the main reason for significantly higher failure rates.

Failure was six times more frequent in the maxilla, and failures in the maxilla occurred faster after placement than in the mandible. Hypothetically, this can be explained by the thin bone in the maxilla compared to the thicker cortical bone of the mandible. In addition, the age of the patient correlated with the failure rate (Table 4.2). This observation is important when considering placement of miniplates at a young age. When treatment is started at a later age, less skeletal effect could be expected because the circumzygomatic and circummaxillary sutures are less open, thus allowing less traction and bone apposition. The mean age of placement in our study was 11.4 years. Using 11 years as a cut-off, we found a non-significant difference in the younger group (i.e., more failure). Traditional facemask treatment is advised to start at around 8 years old to achieve the maximum skeletal effect. In a previous study, early protraction of the maxilla by a facemask reduced the need for adjuvant orthognathic surgery compared a control group without traction; 36% of the facemask patients required orthognathic surgery compared to 66% of the patients without traction when subjectively analyzing the facial profile [11].
A solution that has gained popularity is the use of hybrid hyrax system anchored on two anteriorly placed palatal mini-implants, supposedly giving more traction and opening or loosening the circummaxillary sutures [16,37,40]. The hybrid hyrax system is often used with the Mentoplate © system, which is placed in the thick basal bone of the lower mandible. This avoids damage of the lower canines when placed in young patients- as we saw in one of our patients- because the fixation screws are placed under the erupting canines.
Failure of miniplates by fixation screw loosening accounts for 25% of all patients in class III treatment, with significantly more failure in younger patients [39] . In our study, failure rates were significantly lower in patients who received self-drilling screws (13.7%) compared to patients treated with self-tapping screws (38.5%), which is in line with animal studies [41,42]. Hibi et al. (2006) [43] showed that self-drilling screws are better than self-tapping screws for locking plates in the maxilla. Self-drilling screws give more primary stability and avoid some of the problems of predrilling holes for self-tapping screws, such as thermal or mechanical damage to the bone. In addition, predrilling can result in perforation of the maxillary sinus and, when returning the pilot drill, microorganisms of the inner surface of the maxillary sinus can contaminate

the operation field. When using short self-drilling screws with a maximum length of 5 mm in the maxilla, there is less chance of penetration of the maxillary sinus and, even when the screw tip penetrates the sinusal mucosa, only the screw tip will be contaminated and not the whole operation area [43].

The main goal of class III elastic traction is correction of the class III skeletal relationship. This can be achieved by protraction of the maxilla and prevention of mandibular growth. The advancement of A-point gives information about the forward movement of the maxilla and is already demonstrated for facemask use (+2.3 mm). For BAMP on four miniplates, only case series with a small number of patients were available until now, with results of +5.2 mm. The movement of A-point was only +1.6 mm in this study, but it provides no information about the correction of the class III relationship itself. Therefore, ANB and Wits analysis are key parameters [33,44].

Various growth studies have reported that SNA, the angle of maxillary prognathism, remains constant throughout growth [16]. In our study, SNA had a mean positive change of 1.9°, which is less than the 2.1° - 2.7° change reported in the literature [45]. SNB had a positive change of 0.4° compared to a decrease of 3.1° in the literature, but a previous study reported that SNB and ANB changes were not significant when compared to facemask traction [4]. The decrease in the position of B-point in the literature is explained by horizontal backward movement of the mandible with relocation of the condyle in the glenoid fossa and prevention of mandibular growth [8,46]. Hypothetically, the unchanged mandibular position after BAMP in our study can be explained by the prevention of mandibular growth due to elastic traction. Previous studies confirm that SNB is not predictably stable after treatment due to further mandibular growth [47].

A recent systematic review and meta-analysis [4] compared skeletal correction between patients with four miniplates and patients with a facemask. The Wits value significantly increased by 1.28 mm and SNA by 0.60° with miniplates compared to facemask, proving the superiority of class III traction with miniplates[4]. Systematic reviews by Jamilian et al. (2016) [48] and Feng et al. (2012)[9] demonstrated even more protraction of the maxilla using skeletal anchorage, which we cannot confirm in our study. In addition, many side effects were reduced, as they observed less mandibular rotation and no extrusion of the upper molars or proclination of the upper incisors. Ge et al. (2012) [47] concluded that skeletal-anchored maxillary protraction reduces relapse because the advancement is strictly skeletal without dentoalveolar movements. A three-dimensional cone-beam computed tomography study of 25 patients showed anterior displacement of the maxilla by 3.73 mm with similar anterior displacement of the zygomas and infraorbital rim, which proves the protraction of the midface as a unit by stimulating the circummaxillary (e.g., pterygomaxillary fissure) and circumzygomatic sutures [35]. There is also minimal counterclockwise rotation of the maxilla. This contradicts with the hypotheses of Teuscher, who says there is a center of resistance located at the maxillary buttress [49]. Other studies have shown that the center of resistance is located between the root tips of the first and second maxillary molars, or between the first and second premolars, or even 5 mm above the nasal floor [25,50,51].

Comparing preoperative parameters, we noticed that our patients had less of a class III relationship than stated in the inclusion criteria of other reports. Unlike other studies, we also included treated patients with only a tendency for class III. This may be why we found less skeletal correction based on ANB and Wits analysis. The mean preoperative Wits value for our patients (-4.3 mm) was lower than previous studies, which reported an initial Wits analysis of -4.8 mm in 26 patients to -5.1 mm in 14 patients [8,26,35,45]. The present study is the first multicenter study (multi-surgeon, multi-orthodontist) reporting the outcome of the BAMP protocol. Because of this, our results may better represent the expected results using miniplates for class III skeletal correction.

CONCLUSION

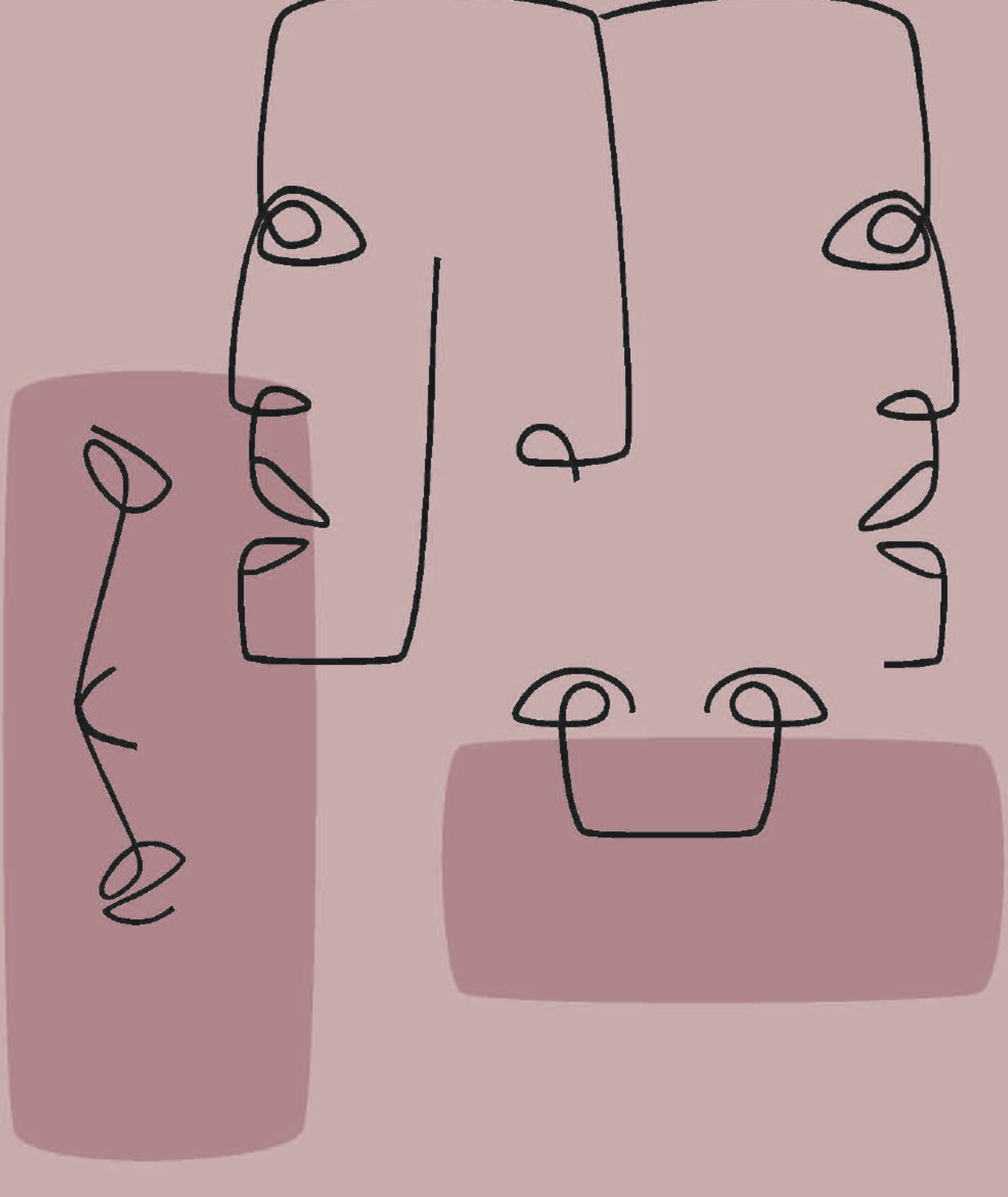
Bone-anchored maxillary protraction is an effective treatment option for correcting class III skeletal relationships The survival rate for miniplates in this study was 93.6%, and 25.7% of the patients suffered failure of one of the miniplates. A significant difference was found between the participating centers in the failure rate of bone anchors. When postoperative antibiotics were used and the neck of the bone anchor placed in the attached gingiva, failure rates were less. Miniplates placed in the maxilla failed six times as often as mandibular miniplates, and self-drilling screws had significantly fewer failures than self-tapping screws for fixing the miniplate. Furthermore, cephalometric analysis revealed less skeletal effect than previously reported in the literature.

REFERENCES

1. Mills, L. F. Epidemiologic studies of occlusion. IV. The prevalence of malocclusion in a population of 1,455 school children. *J Dent Res* 45, 332–336 (1966).
2. Willems, G., De Bruyne, I., Verdonck, A., Fieuws, S. & Carels, C. Prevalence of dentofacial characteristics in a belgian orthodontic population. *Clin Oral Investig* 5, 220–226 (2001).
3. Soh, J., Sandham, A. & Chan, Y. H. Occlusal status in Asian male adults: prevalence and ethnic variation. *Angle Orthod* 75, 814–820 (2005).
4. Rodríguez de Guzmán-Barrera, J. *et al.* Effectiveness of interceptive treatment of class III malocclusions with skeletal anchorage: A systematic review and meta-analysis. *PLoS One* 12, e0173875 (2017).
5. Woon, S. C. & Thiruvenkatachari, B. Early orthodontic treatment for Class III malocclusion: A systematic review and meta-analysis. *Am J Orthod Dentofacial Orthop* 151, 28–52 (2017).
6. Ellis III, E. & McNamara Jr., J. A. Components of adult class III malocclusion. *Journal of Oral and Maxillofacial Surgery* 42, 295–305 (1984).
7. Baik, H. S., Han, H. K., Kim, D. J. & Proffit, W. R. Cephalometric characteristics of Korean Class III surgical patients and their relationship to plans for surgical treatment. *Int J Adult Orthodon Orthognath Surg* 15, 119–128 (2000).
8. T., B., H.J., D. C., L.H., C. & L., F. Morphometric analysis of treatment effects of bone-anchored maxillary protraction in growing Class III patients. *Eur J Orthod* 33, 121–125 (2011).
9. Feng, X. *et al.* Effectiveness of TAD-anchored maxillary protraction in late mixed dentition: A systematic review. *Angle Orthodontist* 82, 1107–1114 (2012).
10. Yang, X. *et al.* Treatment effectiveness of Fränkel function regulator on the Class III malocclusion: a systematic review and meta-analysis. *Am J Orthod Dentofacial Orthop* 146, 143–154 (2014).
11. Mandall, N. *et al.* Early class III protraction facemask treatment reduces the need for orthognathic surgery: a multi-centre, two-arm parallel randomized, controlled trial. *J Orthod* 43, 164–175 (2016).
12. Deguchi, T. & McNamara, J. A. Craniofacial adaptations induced by chincup therapy in Class III patients. *Am J Orthod Dentofacial Orthop* 115, 175–182 (1999).
13. Abu Alhaija, E. S. & Richardson, A. Long-term effect of the chincap on hard and soft tissues. *Eur J Orthod* 21, 291–298 (1999).
14. Delaire, J. [Treatment of Class III with dentofacial orthopedic mask]. *Acta Odontol Venez* 17, 168–200 (1979).
15. Vermeulen, F. M. J., De Clerck, H. J., van Beek, H. & Becking, A. G. [Interceptive treatment of maxillary hypoplasia with the use of bone anchors. A review of the literature]. *Ned Tijdschr Tandheelkd* 121, 91–6 (2014).
16. Kim, J. H., Viana, M. a, Graber, T. M., Omerza, F. F. & BeGole, E. a. The effectiveness of protraction face mask therapy: a meta-analysis. *Am J Orthod Dentofacial Orthop* 115, 675–685 (1999).
17. Mandall, N. *et al.* Is early class III protraction facemask treatment effective? A multicentre, randomized, controlled trial: 15-month follow-up. *J Orthod* 37, 149–161 (2010).
18. Zhang, W., Qu, H. C., Yu, M. & Zhang, Y. The effects of maxillary protraction with or without rapid maxillary expansion and age factors in treating Class III malocclusion: A meta-Analysis. *PLoS One* (2015) doi:10.1371/journal.pone.0130096.
19. Kokich, V. G., Shapiro, P. A., Oswald, R., Koskinen-Moffett, L. & Clarren, S. K. Ankylosed teeth as abutments for maxillary protraction: a case report. *Am J Orthod* 88, 303–307 (1985).
20. Singer, S. L., Henry, P. J. & Rosenberg, I. Osseointegrated implants as an adjunct to facemask therapy: a case report. *Angle Orthod* 70, 253–262 (2000).

21. Enacar, A., Giray, B., Pehlivanoglu, M. & Iplikcioglu, H. Facemask therapy with rigid anchorage in a patient with maxillary hypoplasia and severe oligodontia. *Am J Orthod Dentofacial Orthop* 123, 571–7 (2003).
22. Hong, H., Ngan, P., Han, G. L., Liu, G. Q. & Wei, S. H. Y. Use of onplants as stable anchorage for facemask treatment: A case report. *Angle Orthodontist* 75, 453–460 (2005).
23. Kircelli, B. H., Pektaş, Z. O. & Uçkan, S. Orthopedic protraction with skeletal anchorage in a patient with maxillary hypoplasia and hypodontia. *Angle Orthodontist* 76, 156–163 (2006).
24. Kaya, D., Kocadereli, I., Kan, B. & Tasar, F. Effects of facemask treatment anchored with miniplates after alternate rapid maxillary expansions and constrictions; a pilot study. *Angle Orthod* 81, 639–46 (2011).
25. Sar, C., Sahinoğlu, Z., Özçirpici, A. A. & Uçkan, S. Dentofacial effects of skeletal anchored treatment modalities for the correction of maxillary retrognathia. *Am J Orthod Dentofacial Orthop* 145, 41–54 (2014).
26. Ngan, P. *et al.* Comparison of two maxillary protraction protocols: tooth-borne versus bone-anchored protraction facemask treatment. *Prog Orthod* 16, 26 (2015).
27. Melsen, B. & Melsen, F. The postnatal development of the palatomaxillary region studied on human autopsy material. *Am J Orthod* 82, 329–342 (1982).
28. Baccetti, T. & Tollaro, I. A retrospective comparison of functional appliance treatment of Class III malocclusions in the deciduous and mixed dentitions. *Eur J Orthod* 20, 309–317 (1998).
29. Franchi, L., Baccetti, T. & McNamara, J. A. Postpubertal assessment of treatment timing for maxillary expansion and protraction therapy followed by fixed appliances. *Am J Orthod Dentofacial Orthop* 126, 555–568 (2004).
30. B.H., K. & Z.Ö., P. Midfacial protraction with skeletally anchored face mask therapy: A novel approach and preliminary results. *American Journal of Orthodontics and Dentofacial Orthopedics* 133, 440–449 (2008).
31. De Clerck, H. J., Cornelis, M. A., Cevidanes, L. H., Heymann, G. C. & Tulloch, C. J. F. Orthopedic traction of the maxilla with miniplates: a new perspective for treatment of midface deficiency. *J Oral Maxillofac Surg* 67, 2123–2129 (2009).
32. De Clerck, E. E. B. & Swennen, G. R. J. Success rate of miniplate anchorage for bone anchored maxillary protraction. *Angle Orthodontist* 81, 1010–1013 (2011).
33. Cevidanes, L., Baccetti, T., Franchi, L., McNamara, J. A. & De Clerck, H. Comparison of two protocols for maxillary protraction: bone anchors versus face mask with rapid maxillary expansion. *Angle Orthod* 80, 799–806 (2010).
34. Cornelis, M. A., Scheffler, N. R., Nyssen-Behets, C., De Clerck, H. J. & Tulloch, J. F. C. Patients' and orthodontists' perceptions of miniplates used for temporary skeletal anchorage: a prospective study. *Am J Orthod Dentofacial Orthop* 133, 18–24 (2008).
35. Nguyen, T. *et al.* Three-dimensional assessment of maxillary changes associated with bone anchored maxillary protraction. *American Journal of Orthodontics and Dentofacial Orthopedics* (2011) doi:10.1016/j.ajodo.2011.04.025.
36. Cornelis, M. A. *et al.* Modified miniplates for temporary skeletal anchorage in orthodontics: placement and removal surgeries. *J Oral Maxillofac Surg* 66, 1439–1445 (2008).
37. Mathur, A., Toshniwal, N. G., Kharbanda, O. P. & Thakur, A. Bone anchored maxillary protraction. *American journal of orthodontics and dentofacial orthopedics : official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics* vol. 141 530–532 Preprint at https://doi.org/10.1016/j.ajodo.2012.03.003 (2012).
38. Schätzle, M., Männchen, R., Zwahlen, M. & Lang, N. P. Survival and failure rates of orthodontic temporary anchorage devices: a systematic review. *Clin Oral Implants Res* 20, 1351–1359 (2009).

39. Mommaerts, M. Y., Nols, V. & De Pauw, G. Long-term prospective study of an orthodontic bone anchor. *Int J Oral Maxillofac Implants* 29, 419–426 (2014).
40. Wilmes, B., Nienkemper, M., Ludwig, B., Kau, C. H. & Drescher, D. Early Class III treatment with a hybrid hyrax-mentoplate combination. *J Clin Orthod* 15–21 (2011).
41. Kim, J.-W., Ahn, S.-J. & Chang, Y.-I. Histomorphometric and mechanical analyses of the drill-free screw as orthodontic anchorage. *Am J Orthod Dentofacial Orthop* 128, 190–194 (2005).
42. Wilmes, B. & Drescher, D. Impact of bone quality, implant type, and implantation site preparation on insertion torques of mini-implants used for orthodontic anchorage. *Int J Oral Maxillofac Surg* 40, 697–703 (2011).
43. Hibi, H., Ueda, M., Sakai, M. & Ikemori, Y. Orthodontic anchorage system using a locking plate and self-drilling screws. *J Oral Maxillofac Surg* 64, 1173–1175 (2006).
44. Elnagar, M. H. *et al.* Three-dimensional assessment of soft tissue changes associated with bone-anchored maxillary protraction protocols. *American Journal of Orthodontics and Dentofacial Orthopedics* 152, 336–347 (2017).
45. Katyal, V. *et al.* The efficacy of Hybrid Hyrax-Mentoplate combination in early Class III treatment: a novel approach and pilot study. *Aust Orthod J* 32, 88–96 (2016).
46. De Clerck, H., Nguyen, T., de Paula, L. K. & Cevidanes, L. Three-dimensional assessment of mandibular and glenoid fossa changes after bone-anchored Class III intermaxillary traction. *Am J Orthod Dentofacial Orthop* 142, 25–31 (2012).
47. Ge, Y. S., Liu, J., Chen, L., Han, J. L. & Guo, X. Dentofacial effects of two facemask therapies for maxillary protraction Miniscrew implants versus rapid maxillary expanders. *Angle Orthodontist* 82, 1083–1091 (2012).
48. Jamilian, A., Cannavale, R., Piancino, M. G., Eslami, S. & Perillo, L. Methodological quality and outcome of systematic reviews reporting on orthopaedic treatment for class III malocclusion: Overview of systematic reviews. *J Orthod* 43, 102–120 (2016).
49. Teuscher, U. An appraisal of growth and reaction to extraoral anchorage Simulation of orthodontic-orthopedic results. *Am J Orthod* 89, 113–121 (1986).
50. Hata, S. *et al.* Biomechanical effects of maxillary protraction on the craniofacial complex. *Am J Orthod Dentofacial Orthop* 91, 305–311 (1987).
51. Tanne, K. *et al.* Three-dimensional model of the human craniofacial skeleton: method and preliminary results using finite element analysis. *J Biomed Eng* 10, 246–252 (1988).



SECTION 3 : Facemask treatment versus
Mentoplate treatment protocols.
A 5 year randomized controlled trial.

CHAPTER 5
Overall 2D assessment, comparison with existing evidence

This chapter is based on the following manuscript.

Meyns J., Meewis J., Dons F., Schreurs A., Aerts J., Shujaat S, Politis C., Jacobs R. Long-term Comparison of Maxillary Protraction with Hybrid Hyrax-Facemask vs Hybrid Hyrax-Mentoplate Protocols Using Alt-RAMEC: A 5-Year Randomized Controlled Trial.
European Journal of Orthodontics, Vol 47 (2) April 2025.

ABSTRACT

Background:

The study aimed to compare the short- and long-term effectiveness of hybrid Hyrax (HH) -Facemask (FM) and HH-mentoplate (MP) treatment protocols for maxillary protraction using Alt-RAMEC.

Methods:

A single-center 2-arm parallel randomized controlled trial.

Participants: 28 skeletal class III patients (female: 14, male: 14; average age: 9.7 ± 1.3 years;) were included

Interventions: Two treatment groups where protraction therapy was combined with Alt-RAMEC. Group 1: Facemask group (Hybrid Hyrax + Facemask) and Group 2: Mentoplate group (Hybrid Hyrax + Mentoplate).

Objective: To compare skeletal and dental changes between groups using low dose computed tomography (CT) scan from which virtual lateral cephalograms were generated.

Outcome: Outcomes include changes in Wits appraisal (primary outcome), and cephalometric analysis of skeletal and dental changes (secondary outcomes) at 1 year and 5 years after treatment initiation.

Randomization: 28 patients were allocated to either treatment-protocols using sequentially numbered opaque, sealed envelopes. The randomization sequence was generated with a 1:1 allocation ratio.

Blinding: Due to the nature of the trial, the operator and children could not be blinded to the treatment allocation. However, blinding was used when assessing the outcomes.

Results:

Follow-up: one patient was lost at the one-year follow-up and an additional three patients were lost at the 5-year follow-up.

Outcomes: Both treatment protocols effectively improved intermaxillary relationship. Wits measurements showed improvements of 4.42 mm (FM) and 2.86 mm (MP) at T1, decreasing slightly to 3.33 mm (FM) and 1.50 mm (MP) at T2. While vertical control and incisor inclination were comparable between groups long-term, short-

term differences were noted in upper and lower incisor inclination. Results remained equally stable after five years (T2).

Harms: minor harms were encountered with the anchor hooks (fracture or mucosal irritation), however none led to treatment cessation

Conclusions:

Early class III treatment with HH + MP provided similar outcomes and stability to that of HH + FM suggesting that the choice between FM and MP should be based on individual patient factors rather than presumed mechanical advantages.

INTRODUCTION

Background

The treatment of growing skeletal Class III patients is often viewed as one of the most challenging orthodontic issues. This is due to the unpredictable growth potential of the maxilla and the possibility of unfavorable mandibular growth. It is difficult for an orthodontist to predict the magnitude and timing of skeletal growth. Moreover, the eligibility of patients for early Class III treatment remains a subject of debate [1–3]. One of the most prevalent orthopedic treatment options for early Class III correction is facemask (FM) therapy alone or in combination with rapid palatal expansion (RPE) appliance. However, this method has undesirable side effects such as dentoalveolar compensation, minimal skeletal effect, and unwanted vertical changes [4].

In recent years, several techniques for orthopedic treatment with skeletal anchorage devices have gained popularity [5–18] . These devices have been suggested to reduce the adverse effects associated with FM therapy and even successfully treat large Class III deformities [3,5,6,10,19–26] . Despite the widespread use of skeletal anchorage for interceptive Class III treatment, there is currently no consensus on indications, techniques, age, protocols, or forces employed [2,27,28] . Furthermore, skeletal anchorage procedures do come with possible drawbacks: they involve more or less invasive procedures to place and subsequently remove the devices. Also, some miniscrews and bone anchors are not stable throughout treatment [10,29]. Whether bone-anchors provide better long-term stability of the treatment effect is unknown, due to the lack of evidence at this moment [27,30,31]

Amongst the anchorage devices, Hybrid Hyrax appliance (HH) has been successfully implemented, which uses two mini-implants in the anterior palate to provide skeletal anchorage for maxillary protraction during simultaneous rapid palatal expansion (RPE) [32,33].

The effectiveness of Rapid Palatal Expansion (RPE) for maxillary protraction remains debated [34,35], though it may enhance skeletal effects by mobilizing midfacial sutures. The Alternate Rapid Maxillary Expansion and Constriction (Alt-RAMEC) protocol claims to achieve greater and faster skeletal changes by further stimulating upper jaw growth through circummaxillary suture opening [36,37]. Meta-

analysis shows that Alt-RAMEC combined with bone-anchored appliances produces superior sagittal skeletal effects while minimizing vertical and dentoalveolar changes [38]. However, recent research indicates that while skeletal anchorage in HH improves both sagittal and vertical skeletal effects, the addition of Alt-RAMEC to these devices shows no added benefit [33]. Therefore, the value of combining Alt-RAMEC with HH remains uncertain.
When considering the lower jaw, the use of bone-anchors, such as mentoplate (MP) in combination with maxillary HH [39–41] have also been hypothesized to produce more skeletal effect due to the direct transfer of force on the bone and potentially better patient compliance, however no evidence was found to support this theorem. [3,27,30,42]. Such a skeletal anchorage with symphyseal plates in the lower jaw could provide greater vertical control and might be the treatment of choice in high-angle patients [43–45] . However, lack of evidence exists assessing the efficacy of HH+MP in comparison to the conventional HH+FM therapy. Most studies on skeletal anchorage techniques are either clinical cases or case series, with a notable lack of randomized controlled trials (RCTs) [3,27,30,31]. Furthermore, the long-term stability of the treatment effect provided by bone-anchors is yet to be explored [46].

Objectives

Therefore, the objective of this prospective RCT was to compare the short- (1 year) and long-term (5 years) effectiveness of HH+FM and HH+MP therapy with Alt-RAMEC-protocol in growing Class III patients by assessing the CT-derived two-dimensional (2D) cephalometric variables.

METHODS

Trial design

Single-center 2-arm parallel randomized controlled trial with 1:1 allocation ratio.

Participants

This study examined patients with Class III skeletal malocclusion that were referred to our hospital by their orthodontist. All participants were in mixed dentition with anterior crossbite or an end-to-end incisor relationship and Class III molar relationship at start of treatment. Patients were excluded if they had cleft/craniofacial syndromes, prior orthodontic/surgical treatment, significant skeletal asymmetry, or functional Class III malocclusion. A single surgeon performed HH screw and MP placements, while three experienced orthodontists provided orthodontic care.

Interventions

Palatal expansion by HH

In each patient, two self-drilling mini-screws (each 2 mm in diameter and 9 mm in length, sourced from Benefit miniscrews, PSM-medical solutions®, Gunningen, Germany) were implanted into the anterior palate around the third rugae. A Hybrid Hyrax (HH) apparatus was assembled with an expansion screw (Forestadent ®) and affixed to bands. These bands were subsequently cemented to the first upper molars using a light-cured cement (Band-Lok, Reliance Orthodontic Products ®, Thorndale, USA) (Figure 5.1, Figure 5.2). The Alternate Rapid Maxillary Expansion and Constriction (Alt-RAMEC) protocol was employed [47], wherein the HH was activated by the patient's parents twice daily (0.25 mm per turn, two turns in the morning and two turns at night) for one week, followed by deactivation twice daily (two turns in the morning and two turns at night) for the next week. This cycle of alternating activation and deactivation was repeated three times. In the following week, the maxilla was adjusted to the suitable transverse dimension.

FM group

In this group, Facemask (FM) therapy commenced concurrently with Alt-RAMEC. Elastics were connected from the hooks of the expander to the FM (Orthocomfort & Medical Distributors SL®, Barcelona, Spain), creating a downward and forward vector (Figure 5.1). This configuration produced orthopedic forces of 360 - 400 g per side (equivalent to 12,7 – 14 oz). The patients were instructed to use the device for 12–14 hours daily, primarily overnight, for the initial six months or until they achieved a positive overjet of at least 2 mm. For the following six months, the FM was to be worn only during sleep. (Figure 5.1)

MP group

Following general anesthesia, a mentoplate (MP) (PSM-medical solutions®, Gunningen, Germany) was inserted through a marginal gingival incision. The plate was bent and modified prior to fixation with two to four screws (KLS Martin®, Tuttlingen, Germany) (Figure 5.2). The patients were simultaneously provided with Alt-RAMEC and protraction elastics, generating orthopedic forces of 185 g per side (equivalent to 6 ½ oz). The patients were advised to wear it continuously, 24 hours a day, 7 days a week, including during meals. They were also instructed to replace the elastics daily for the first six months or until a positive overjet of at least 2 mm was achieved. For the subsequent six months, the elastics were to be worn only during sleep. (Figure 5.2)

Fixed appliances

During phase 1, only protraction therapy was used, with no fixed appliances present at T1. All patients later received identical full fixed orthodontic appliances (edgewise mechanics, MBT .022 slot, Empower R, American Orthodontics ®) during phase 2. Also no elastic traction was employed during phase 2, after the one year (T1) time-point. The treating orthodontists followed standardized techniques for both treatment phases.

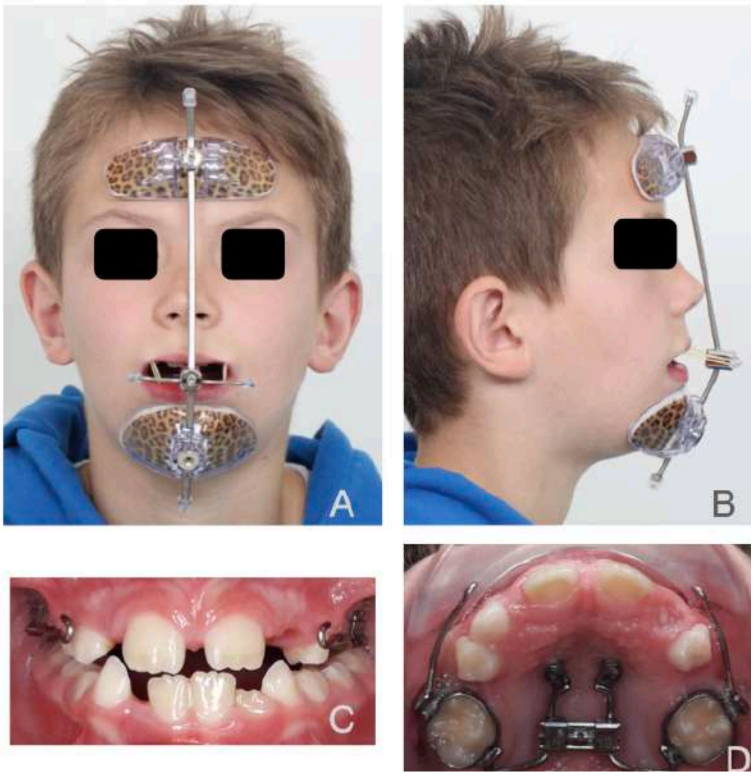


Figure 5.1: Facemask treatment.
A. Frontal view; B. Lateral view; C. Intra-oral frontal view;
D. Occlusal view hybrid hyrax

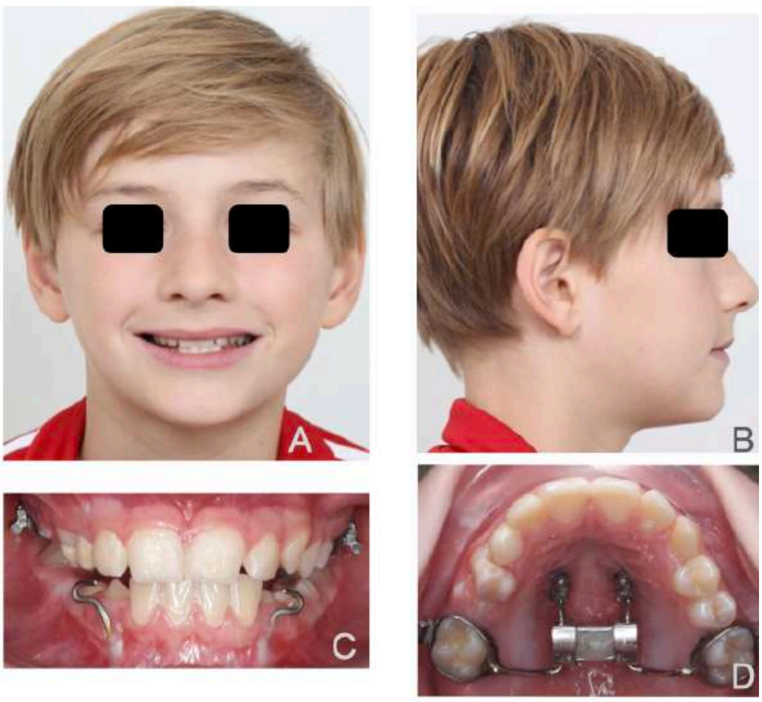


Figure 5.2: Mentoplate treatment.
A. Frontal view; B. Lateral view; C. Intra-oral frontal view;
D. Occlusal view hybrid hyrax

Outcomes

Outcomes include changes in Wits appraisal (primary outcome), and cephalometric analysis of skeletal and dental changes (secondary outcome) at 1 year and 5 years after treatment initiation. No changes were made after trial commencement.

Radiographic data acquisition

A single radiology technician performed low-dose CT scans at three intervals: baseline (T0), one-year post-treatment (T1), and five years post-treatment (T2). During scanning, patients lay supine with a wax bite in centric relation (in first tooth contact) and were instructed to remain still, breathe normally, and avoid swallowing. Scans were performed using a Somatom Force dual-source dual-energy CT system (Siemens®, Erlangen, Germany) with the following parameters: - 0.6 mm slice thickness - 0.3 mm increment - 1.0 pitch - 200 x 200 mm field of view - 150 kVp tube voltage. The machine and parameter settings allowed better image quality and faster acquisition times, resulting in fewer motion artifacts and low radiation doses considering an automatic dose modulation protocol. Effective radiation doses for the applied CT were comparable to CBCT doses and ranged from 0.095 to 0.257 mSv per scan.

Cephalometric analysis

The cephalometric images were generated from the T0, T1 and T2 CT datasets with Planmeca Romexis software (version 6.3.0, Planmeca®, Helsinki, Finland), using an orthogonal method without magnification. The cephalograms were superimposed on the cranial base and cephalometric analysis was conducted at all time-points with the OnyxCeph software (version 3.6, Image Instruments GmbH®, Chemnitz, Germany). The cephalometric variables used in this study are listed in Table 5.2 and depicted in Figure 5.3 , 5.4 and 5.5. Two independent oral and maxillofacial surgery trainees analyzed 10% of the data twice at an interval of two weeks to determine the inter- and intra-observer reliability.

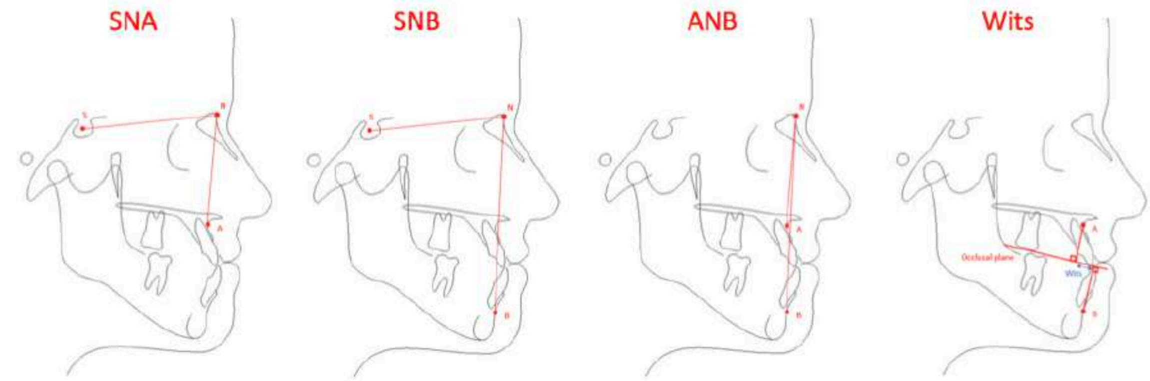


Figure 5.3: Sagittal cephalometric measurements evaluated in this study: SNA, SNB, ANB and Wits

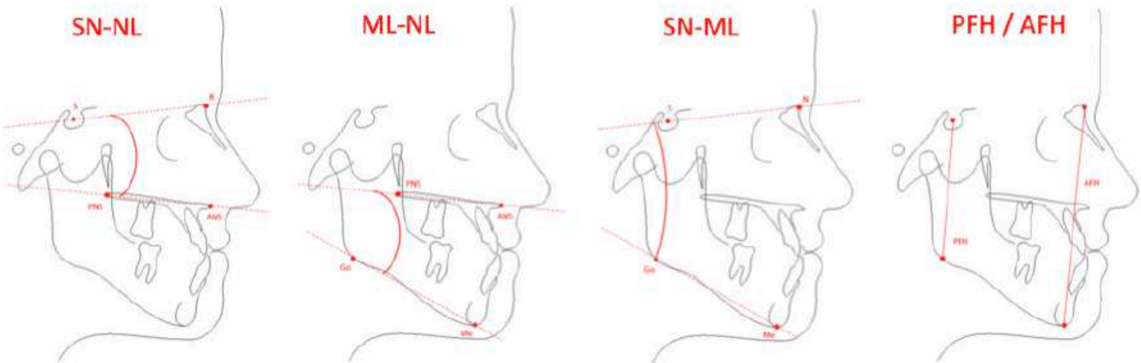


Figure 5.4: Rotational measurements evaluated in this study: SN-NL, ML-NL, SN-ML and PFH/AFH

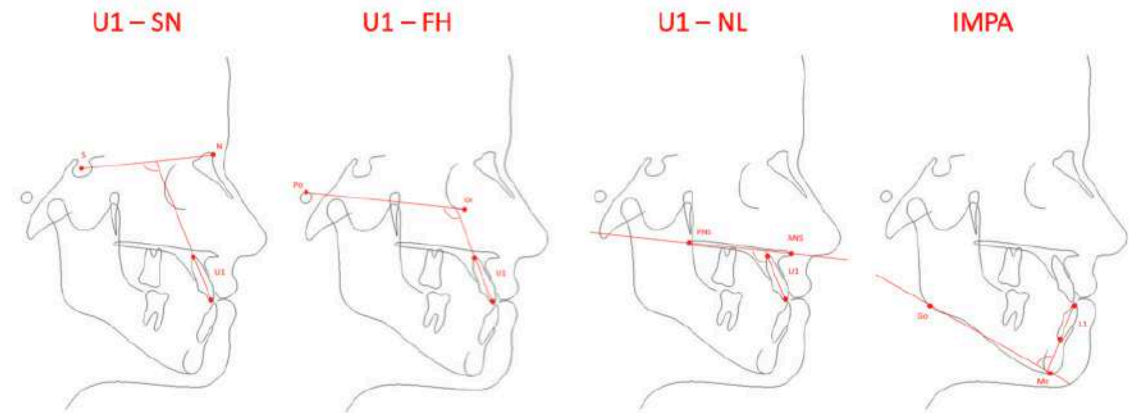


Figure 5.5: Dental measurement evaluated in this study: U1–SN; U1-FH; U1-NL; IMPA

Sample Size calculation

When this trial began, no comparative studies of these specific techniques existed. In 2010 Cevidanes et al. [5] conducted a controlled clinical trial comparing Bone Anchored Maxillary Protraction (BAMP) with Facemask and Rapid Maxillary Expansion (FM-RME), finding a mean Wits difference of 2.3 mm between groups. We pooled the standard deviations from both groups by first converting them to variances by squaring the standard deviations, then taking the average, and converting the average back to a standard deviation by taking the square root. A sample size calculation was performed for a one-sided t-test with a significance level of 0.05 and a power of 80%. This resulted in a required sample size of 12 patients per group. R version 4.1.2 was used, with the TrialSize library to calculate the sample size. We slightly overrecruited to account for potential dropouts.

Randomization

Sequence generation

The randomization sequence was generated with a 1:1 allocation ratio. (for complete data, supplementary file 1)

Allocation concealment

Sequentially numbered sealed, opaque envelopes.

Implementation

The envelopes containing the allocation sequence codes were given to the patient by an intermediary and opened sequentially at the time of enrollment, excluding the clinician from the process.

Blinding

Due to the nature of the trial, the operator and children could not be blinded to the treatment allocation. However, blinding was used when assessing the outcomes. This was achieved by pseudonymizing all patient data before and after treatment. The statistician analyzing the results was unaware of the group assignments.

Statistical analysis

R version 4.1.2 was used, with the TrialSize library for statistical analysis. A normal quantile plot of the residual values showed that they were normally distributed. Homoscedasticity was tested visually by a residual dot plot. The inter- and intra-observer reliability of cephalometric analysis was evaluated using the Intra-Class Correlation Coefficient (ICC) at a 95% confidence interval. The data was descriptively analyzed using the median and standard deviation.

Unpaired two-sided samples t-test was employed for comparisons between two independent samples. A p-value of <0.05 was considered as statistically significant. (Online repository for complete statistical code).

RESULTS

Participants flow

One patient, initially assigned to the MP group, was later excluded due to non-cooperation leading to discontinuation of treatment. Three additional patients, two from the FM group and one of the MP group, were lost to follow-up before the 5-year time-point (Figure 5.6).

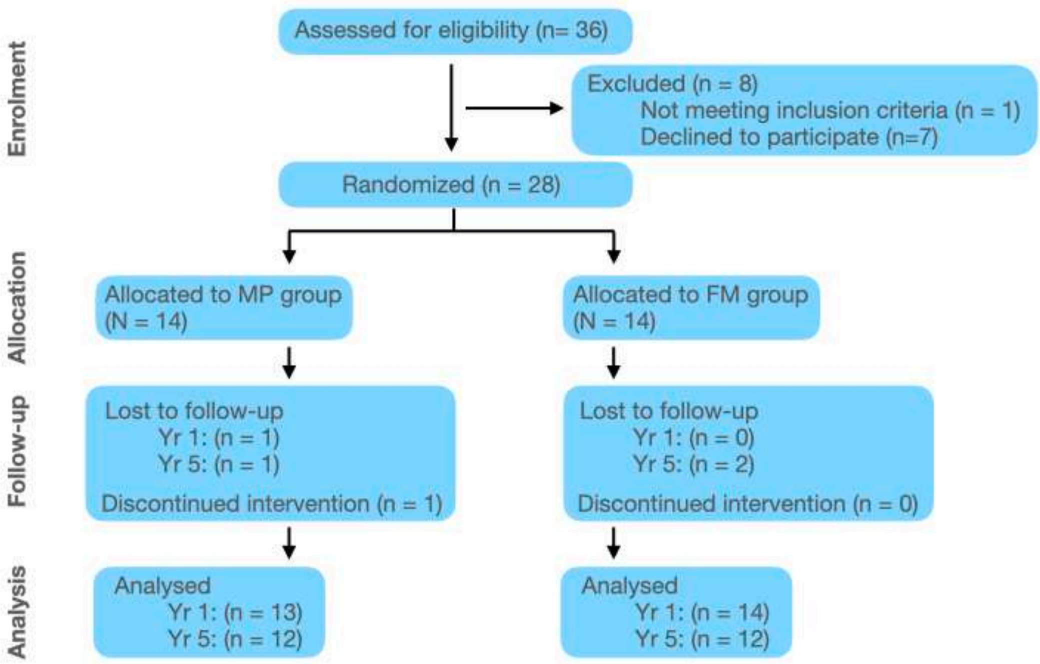


Figure 5.6: Flow diagram of patients' allocations in the trial

Recruitment

Patient recruitment occurred from December 2016 to September 2018. Scans were performed in three phases: initial scans (T0) from February 2017 to September 2018, first follow-up (T1) from February 2018 to August 2019, and second follow-up (T2) from October 2022 to February 2024. (supplementary file 1 for more details)

Baseline data

Twenty-eight patients (14 males, 14 females; mean age 9.7 ± 1.3 years) participated in the study. The FM and MP groups were age- and gender-matched (Table 5.1). Most patients were at CVMI stages 2 or 3, with one patient at stage 1. Initial Class III malocclusion severity was comparable between groups (Table 5.2; supplementary files 2 and 3 for complete data). The randomization process was adhered to rigorously, and there was no violation. The baseline comparisons are provided solely for descriptive purposes and not to infer statistical significance, in alignment with CONSORT principles.

Numbers analyzed.

Twenty-eight patients (14 FM, 14 MP) underwent low dose CT at baseline (T0). At one year (T1), 27 patients (14 FM, 13 MP) completed follow-up scans. By five years (T2), 24 patients (12 FM, 12 MP) remained for analysis (Figure 5.6 and Table 5.1).

Table 5.1: Number, Age and duration of treatment

	N (Female/Male)			Age (mean)			Duration of treatment (mean in months)	
Group	T0	T1	T2	T0	T1	T2	T0-T1	T0-T2
FM	14 (7 / 7)	14 (7/ 7)	12 (7/ 5)	9 y, 6 mo	10 y, 0 mo	15 y, 5 mo	12 mo	64 mo
MP	14 (7 / 7)	13 (6 /7)	12 (5 /7)	9 y, 7 mo	10 y, 7 mo	15 y, 4 mo	11,7 mo	65 mo

FM: Facemask; MP: Mentoplate; T0: baseline; T1: 1 year follow-up; T2: 5 year follow-up

Table 5.2: Group characteristics at baseline (T0).

	Facemask Mean ± SD	**Mentoplate** Mean ± SD	*p-value
Sagittal			
SNA °	79.41 ± 2.43	78.38 ± 3.50	0.38
SNB °	80.22 ± 2.14	78.94 ± 4.25	0.33
ANB °	-0.82 ± 2.03	-0.55 ± 1.45	0.69
Wits (mm)	-5.71 ± 1.82	-5.62 ± 2.36	0.90
Vertical			
SN-ML °	31.71 ± 4.31	35.05 ± 6.08	0.11
SN-NL°	6.49 ± 3.57	8.72 ± 4.32	0.16
NL-ML°	25.2 ± 4.61	26.32 ± 5.84	0.59
PFH/AFH	65.71 ± 3.89	63.00 ± 4.14	0.09
Dental			
U1 -SN	105.53 ± 6.27	104.06 ± 9.27	0.63
U1-FH	118.42 ± 6,70	115.70 ± 9.08	0.38
U1 -NL	113.01 ± 5.65	114.47 ± 7.65	0.58
IMPA	90.41 ± 5.21	91.40 ± 7.27	0.69

*Intergroup comparison is performed using the unpaired two-sided samples t-test. Baseline comparisons are provided for descriptive purposes only, to confirm group equivalence following randomization, and should not be interpreted as inferential statistical analyses.

Outcomes and estimation

Both inter-observer (ICC: 0.96-0.99) and intra-observer (ICC: 0.93-0.99) measurements showed high reliability with no significant differences between observers. Both treatment groups (FM and MP) exhibited similar sagittal and vertical skeletal changes, as shown in Table 5.3. During active treatment (T1-T0), cephalometric analysis revealed maxillary advancement (SNA; FM: + 2.48, MP: + 1.99; p=0.60) and slight mandibular retraction (SNB; FM: -0.86, MP: -0.64; p=0.73). Both ANB (FM: + 3.36, MP: + 2.63; p=0.34) and Wits (FM: + 4.42, MP: + 2.86; p=0.12) measurements showed similar changes in both groups. Post-treatment follow-up (T2-T1) demonstrated comparable relapse patterns in both groups, characterized by mandibular catch-up growth (SNB; FM: + 1.63, MP: + 1.78; p=0.92) and minimal maxillary advancement (SNA; FM: + 0.18, MP: + 0.88; p=0.61). Vertically, no significant jaw rotations occurred during active treatment. However, in phase two, both groups exhibited counterclockwise mandibular rotation (SN-ML; FM: - 3.03, MP: - 1.12; p=0.36), resulting in a slight increase in the posterior-to-anterior facial height ratio (PFH/AFH; FM: + 3.58, MP: + 2.25; p=0.44). During active treatment, incisors responded differently between groups: the MP group showed increased proclination of both upper and lower incisors, while the FM group showed retroclination. These differences were statistically significant (U1-SN: p=0.04, U1-NL: p=0.02, IMPA: p=0.01), though high standard deviations suggest individual responses varied widely. The differences in incisor inclination disappeared during follow-up (T2-T0). Mean follow-up time was 12 ± 1.59 months at T1 and 64.5 ± 5.21 months at T2 (Table 5.1) (for complete data, supplementary file 1).

Ancillary analyses

No ancillary analyses were done.

Harms

In our MP patients' group, no loosening of the plate was observed. Although some issues with the anchor hooks (fracture or mucosal irritation) were encountered, none led to treatment cessation.

Table 5.3: Cephalometric changes in facemask and mentoplate treatment groups

Variable	T1-T0 Mean ± SD			T2-T0 Mean ± SD			T2-T1 Mean ± SD		
	Facemask	**Mentoplate**	p-value	**Facemask**	**Mentoplate**	p-value	**Facemask**	**Mentoplate**	p-value
Sagittal									
SNA °	2.48 ± 2.47	1.99 ± 2.01	0.60	2.65 ± 2.89	2.88 ± 4.14	0.88	0.18 ± 2.60	0.88 ± 3.97	0.61
SNB °	-0.86 ± 1.39	-0.64 ± 1.65	0.73	0.78 ± 2.57	1.14 ± 4.04	0.79	1.63 ± 2.95	1.78 ± 3.96	0.92
ANB °	3.36 ± 2.19	2.63 ± 1.40	0.34	1.90 ± 3.07	1.71 ± 2.65	0.87	-1.46 ± 2.40	-0.93 ± 2.33	0.59
Wits (mm)	4.42 ± 2.11	2.86 ± 2.59	0.12	3.33 ± 2.50	1.50 ± 3.45	0.15	-1.08 ± 2.43	-1.36 ± 3.92	0.84
Vertical									
SN-ML °	0.52 ± 1.48	-0.46 ± 2.05	0.20	-2.52 ± 4.17	-1.58 ± 5.34	0.63	-3.03 ± 4.79	-1.12 ± 5.19	0.36
SN-NL°	-0.18 ± 2.66	-0.71 ± 3.66	0.69	-0.08 ± 2.63	-0.08 ± 5.52	1.00	0.10 ± 3.64	0.63 ± 4.55	0.75
NL-ML°	0.73 ± 2.09	0.24 ± 4.48	0.74	-2.42 ± 4.79	-1.83 ± 5.30	0.78	-3.14 ± 4.45	-2.08 ± 4.53	0.57
PFH/AFH	-0.58 ± 1.44	0.25 ± 1.76	0.22	3.00 ± 4.02	2.50 ± 3.61	0.75	3.58 ± 4.29	2.25 ± 3.93	0.44
Dental									
U1 -SN	-3.44 ± 5.63	1.90 ± 6.26	0.04*	5.74 ± 6.16	5.03 ± 11.14	0.85	9.18 ± 3.92	3.13 ± 7.96	0.03*
U1-FH	-2.90 ± 4.93	2.43 ± 7.55	0.05	5.67 ± 6.93	6.34 ± 11.16	0.86	8.57 ± 4.36	3.92 ± 7.43	0.07
U1 -NL	-4.40 ± 4.86	1.27 ± 6.42	0.02*	5.38 ± 7.10	4.16 ± 12.19	0.77	9.78 ± 4.76	2.89 ± 8.48	0.02*
IMPA	-3.13 ± 4.19	2.49 ± 6.07	0.01*	3.61 ± 7.63	1.42 ± 8.31	0.51	6.74 ± 7.24	-1.08 ± 9.99	0.04*

T1 (1 year), T2 (5 year), FM (facemask), MP (mentoplate). Results are described in median ± standard deviations. Intergroup comparison is performed using unpaired two-sided samples t-test.(T0 was subtracted from T1; T0 was subtracted from T2 and T1 was subtracted from T2. This means that a positive value indicates more protrusion whereas a negative value indicates retrusion)

DISCUSSION

The following study is the first RCT to compare the long-term skeletal and dental effects of FM and MP therapy in combination with HH-Alt-RAMEC. A 2D cephalometric approach was applied instead of three-dimensional analysis as vertical changes and intermaxillary changes are difficult to quantify using 3D volumetric analysis. Moreover, it allowed a more direct comparison with the existing evidence, where lack of 3D values exists in literature.

The comparison of FM and MP groups cephalometric outcomes showed no significant differences in the sagittal and vertical skeletal dimensions. These findings align with prior studies that compared HH with MP and FM at a short-term follow-up without Alt-RAMEC protocol [45] . Despite previous studies suggesting that the use of symphyseal plates could yield improved vertical control [43–45], recent research indicates that vertical control depends primarily on upper jaw anchorage [33]. Our study confirms this finding, as both groups showed effective vertical control during active treatment, despite using different lower jaw anchorage methods but identical HH devices. Effectiveness of Rapid Palatal Expansion (RPE) for maxillary protraction remains debated, though it may enhance skeletal effects by mobilizing midfacial sutures [34,35]. The Alternate Rapid Maxillary Expansion and Constriction (Alt-RAMEC) protocol claims to achieve greater and faster skeletal changes by further stimulating upper jaw growth through circum-maxillary suture opening [33,36,37]. Whether skeletal anchorage through HH in the maxilla produces greater sagittal skeletal effects remains unclear due to conflicting evidence in the literature [33,48,49]. Adding Alt-RAMEC to the HH-device shows no additional advantages [33], which is confirmed in our short term results. Our protocol, using HH with Alt-RAMEC shows similar SNA, SNB, ANB, and wits measurements changes compared to previous studies, using both MP- RPE HH [45] , FM-RPE HH and FM-Alt-RAMEC HH [9,50] . This indicates that Alt-RAMEC does not improve HH treatment outcomes in pre-pubertal patients (CVMI 2-3), compared to RPE with HH. A possible explanation might be that, as the subjects were young and the circum-maxillary sutures were still patent, using skeletally anchored Alt-RAMEC may not have any additional benefit in correcting the sagittal relationship in comparison to skeletal anchored RPE. Our short-term outcomes of Alt-RAMEC protocol using face mask with hybrid hyrax (FM-

HH) showed similar results compared to face mask with tooth-borne expander (FM-TBE) and Alt-RAMEC in prepuptertal patients [33,50]. This suggests that in young patients (CVMI 2-3), using Alt-RAMEC with a TBE may be as effective as skeletal anchorage with hybrid hyrax.

Evidence indicates also less dento-alveolar compensation when HH is used as compared to tooth born expanders (TBE) [4,33,48]. In the short term (T1-T0), incisor inclination differed significantly between the MP and FM groups. The MP group showed mandibular incisor protrusion, while the FM group exhibited retrusion. This was expected and aligns with previous reports [3]. The FM group also showed unexpected maxillary incisor retrusion, while the MP group demonstrated protrusion. Though these differences were statistically significant, there was considerable variation in individual responses as depicted in the amount of SD. By the long term (T2-T0), the FM group's incisor retrusion had reversed due to significant more relapse during phase 2 (U1-SN: $p=0.03$; IMPA: $p=0.04$). No long-term differences in incisor inclination remained between groups (T2). The initial differences likely stemmed from chin cup pressure during treatment, which caused lower incisor retrusion and, through occlusal interaction, upper incisor retrusion in the FM group. These differences disappeared after chin cup pressure was stopped.

Our treatment protocols showed similar or better outcomes compared to other skeletal anchorage methods, including BAMP [51,52] and miniscrew [48,52] protraction. The type of anchorage device appears less important [27] than the patient's age at treatment initiation. Although BAMP protocols typically begin at an older age and include retention therapy during phase 2, our earlier intervention without retention therapy did not lead to increased relapse. In fact, our long-term results were comparable or slightly superior to long term BAMP outcomes [29,51].

The findings of the present study indicated that MP protocol did not yield significantly superior outcomes. The MP’s effectiveness was comparable to that of FM therapy, thereby suggesting that it could serve as a feasible alternative to FM, which is currently viewed as the standard clinical treatment in growing class III patients. The MP protocol could be a suitable alternative when FM may not be the best solution due to compliance issues or anatomical limitations. Despite ongoing debates, initiating treatment at an early age appears to yield more skeletal effects [34–37]. The

MP can be inserted before the eruption of the mandibular canines, facilitating an early commencement of Class III treatment and eliminating the need for FM (Figure 5.7). In terms of the stability of MP as a bone anchor, this treatment option rarely experiences plate loosening, most likely due to the plate's positioning, fixation, and form in the mandible's basal bone. It is a single-piece construction offering simultaneous traction on both sides into the basal bone, thereby preventing plate loosening. In our MP patients' group, no loosening of the plate was observed. Although some issues with the anchor hooks (fracture or mucosal irritation) were encountered, none led to treatment cessation. The inclusion of MP in the orthodontic toolkit is especially recommended when customizing treatment to accommodate each patient's unique needs and preferences. Furthermore, the HH device also showed no loosening of mini-screws during treatment, as these screws are rigidly connected to the HH device. Considering the better vertical control, less dento-alveolar compensations using HH and potential negative effects of TBE-Alt-RAMEC on buccal bone thickness [53], skeletal anchorage with hybrid hyrax is the preferred choice of anchorage in the upper jaw. Alt-RAMEC does not improve the results in young patients, whether this is the case in patients when treatment is started at later age is unknown.

A key factor in both treatment options is patient compliance. It is recommended that patients use the facemask 14 hours a day and intra-oral elastics 24/7 in the first months of treatment. It has been suggested that patient compliance is easier obtained using bone-anchors and intra-oral elastics. As in all other studies, it would have been most desirable being able to objectively measure the exact wear times of the elastics for maxillary protraction.

The strength of the study was the first time prospective RCT-based reporting of the long-term comparison of HH+FM and HH+MP therapy.

Figure 5.7: position of the mentoplate with impacted canines in the lower jaw

Limitations

The study had certain limitations. Firstly, a limited number of patients were included in the study. Although sample size calculation was performed, a larger sample might be required to reach a definitive conclusion owing to the unpredictable growth issues. Significant patient attrition occurred at the five-year follow-up, also in the mentoplate (MP) group. This was unexpected since MP patients typically return for hardware removal. Although all mentoplates were eventually removed, the varied timing of these procedures extended beyond the T2 timepoint. Therefore, these patients did not undergo low dose CT and were excluded from the study to avoid potential bias. Secondly, the outcome analysis was solely based on 2D cephalometry. This approach may oversimplify results by focusing on measurable outcomes while overlooking aesthetic quality and genetic factors. Class III malocclusion is complex, influenced by multiple genes, ethnic background, and environmental factors like muscle function and nutrition [54]. Individual variation in growth patterns and genetic predisposition for class III malocclusion may significantly influence treatment outcomes, regardless of the intervention chosen. Our sample size, while statistically adequate, may not fully represent the spectrum of genetic variability in Class III patients. This randomized controlled trial (RCT) focused specifically on appliance design and mechanics and its findings challenge the common assumption that bone anchors provide superior results despite being more invasive. The study results enable direct comparison with previously published data on this topic. While our 5-year follow-up provides valuable insights, the ultimate stability trough completion of growth cannot be guaranteed, as some patients may experience late mandibular growth. Future studies should focus on 3D cephalometric and volumetric analysis studies, which could serve as a roadmap for virtual 3D diagnosis and treatment planning. Finally, the impact of the treatment protocols on soft tissue was not assessed. It is also recommended to perform future studies for assessing compliance and pain perception associated with MP.

Generalisability

Our results are primarily applicable to patients in the mixed dentition phase (average 9.7 ± 1.3 years) with moderate skeletal discrepancies. The findings may not extend to patients with severe skeletal class III malocclusions or those at different developmental stages.

As this trial was conducted in a single center with an experienced surgeon and orthodontists, results might vary in different clinical settings. We used a standardized Alt-RAMEC protocol and force system. Different expansion protocols or force magnitudes might yield different outcomes.

Interpretation

Early class III treatment with HH+MP skeletal anchorage does not seem to induce a better outcome as compared to HH+FM protocol. The stability of the therapeutic results seems to be consistent for both treatment groups at a long-term follow-up. These findings challenge the common assumption that bone anchors necessarily provide superior results despite being more invasive. This is particularly relevant for clinical decision making, as it suggests that the choice between FM and MP should be based on individual patient factors rather than presumed mechanical advantages.

Other information

Registration

This Randomized Clinical trial was registered at www.ClinicalTrials.gov (ID: NCT02711111) Ethical approval has been granted by the Ethics Committee at the Ziekenhuis Oost Limburg, Belgium (EudraCT B371201629565) (13/12/2016)

Conflicts of interest

The authors declare that they have no conflict of interest.

Data availability

The data used to support the findings of this study are available within the article, its supplementary materials and online repository. (Meyns, Joeri (2025), “Long-term Comparison of Maxillary Protraction with Hybrid Hyrax-Facemask vs Hybrid Hyrax-Mentoplate Protocols Using Alt-RAMEC: A 5-Year Randomized Controlled Trial”, Mendeley Data, V1, doi: 10.17632/2p6mf2fn2f.1)

Funding

No funding was received.

REFERENCES

1. Woon SC, Thiruvenkatachari B. Early orthodontic treatment for Class III malocclusion: A systematic review and meta-analysis. *Am J Orthod Dentofacial Orthop*. 2017;151(1):28-52. doi:10.1016/j.ajodo.2016.07.017
2. De Toffol L, Pavoni C, Baccetti T, Franchi L, Cozza P. Orthopedic Treatment Outcomes in Class III Malocclusion. *Angle Orthodontist*. 2008;78(3). doi:10.2319/030207-108.1
3. Rongo R, D'Antò V, Bucci R, Polito I, Martina R, Michelotti A. Skeletal and dental effects of Class III orthopaedic treatment: a systematic review and meta-analysis. *J Oral Rehabil*. Published online February 18, 2017. doi:10.1111/joor.12495
4. Ngan PW, Hagg U, Yiu C, Wei SH. Treatment response and long-term dentofacial adaptations to maxillary expansion and protraction. *Semin Orthod*. 1997;3(4):255-264. doi:10.1016/S1073-8746(97)80058-8
5. Cevidanes L, Baccetti T, Franchi L, McNamara JA, De Clerck H. Comparison of two protocols for maxillary protraction: bone anchors versus face mask with rapid maxillary expansion. *Angle Orthod*. 2010;80(5):799-806. doi:10.2319/111709-651.1
6. Şar Ç, Şahinoğlu Z, Özçirpici AA, Uçkan S. Dentofacial effects of skeletal anchored treatment modalities for the correction of maxillary retrognathia. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2014;145(1). doi:10.1016/j.ajodo.2013.09.009
7. De Clerck HJ, Proffit WR. Growth modification of the face: A current perspective with emphasis on Class III treatment. *American Journal of Orthodontics and Dentofacial Orthopedics*. Published online 2015. doi:10.1016/j.ajodo.2015.04.017
8. Rodríguez de Guzmán-Barrera J, Sáez Martínez C, Boronat-Catalá M, et al. Effectiveness of interceptive treatment of class III malocclusions with skeletal anchorage: A systematic review and meta-analysis. Bencharit S, ed. *PLoS One*. 2017;12(3):e0173875. doi:10.1371/journal.pone.0173875
9. Nienkemper M, Wilmes B, Franchi L, Drescher D. Effectiveness of maxillary protraction using a hybrid hyrax-facemask combination: *A controlled clinical study*. *Angle Orthod*. 2015;85(5):764-770. doi:10.2319/071614-497.1
10. Bozkaya E, Yüksel AS, Bozkaya S. Zygomatic miniplates for skeletal anchorage in orthopedic correction of Class III malocclusion: A controlled clinical trial. *The Korean Journal of Orthodontics*. 2017;47(2):118. doi:10.4041/kjod.2017.47.2.118
11. Enacar A, Giray B, Pehlivanoglu M, Iplikcioglu H. Facemask therapy with rigid anchorage in a patient with maxillary hypoplasia and severe oligodontia. *Am J Orthod Dentofacial Orthop*. 2003;123(5):571-577. doi:10.1067/mod.2003.S0889540603000520
12. Hong H, Ngan P, Han GL, Liu GQ, Wei SHY. Use of onplants as stable anchorage for facemask treatment: A case report. *Angle Orthodontist*. 2005;75(3):453-460. doi:10.1043/0003-3219(2005)75[453:UOOASA]2.0.CO;2
13. Jamilian A, Showkatbakhsh R. Treatment of maxillary deficiency by miniscrew implants--a case report. *J Orthod*. 2010;37(1):56-61. doi:10.1179/14653121042876
14. Kaya D, Kocadereli I, Kan B, Tasar F. Effects of facemask treatment anchored with miniplates after alternate rapid maxillary expansions and constrictions; a pilot study. *Angle Orthod*. 2011;81(4):639-646. doi:10.2319/081010-473.1
15. Kircelli BH, Pektaş ZO, Uçkan S. Orthopedic protraction with skeletal anchorage in a patient with maxillary hypoplasia and hypodontia. *Angle Orthodontist*. 2006;76(1):156-163. doi:10.1043/0003-3219(2006)076[0156:OPWSAI]2.0.CO;2
16. Lee NK, Yang IH, Baek SH. The short-term treatment effects of face mask therapy in Class III patients based on the anchorage device: miniplates vs

rapid maxillary expansion. *Angle Orthod*. 2012;82(5):846-852. doi:10.2319/090811-584.1

17. Baek SH, Kim KW, Choi JY. New treatment modality for maxillary hypoplasia in cleft patients. Protraction facemask with miniplate anchorage. *Angle Orthod*. 2010;80(4):783-791. doi:10.2319/073009-435.1
18. Sar C, Arman-Özçırpıcı A, Uçkan S, Yazıcı AC. Comparative evaluation of maxillary protraction with or without skeletal anchorage. *Am J Orthod Dentofacial Orthop*. 2011;139(5):636-649. doi:10.1016/j.ajodo.2009.06.039
19. Hino CT, Cevidanes LHS, Nguyen TT, De Clerck HJ, Franchi L, McNamara JA. Three-dimensional analysis of maxillary changes associated with facemask and rapid maxillary expansion compared with bone anchored maxillary protraction. *American Journal of Orthodontics and Dentofacial Orthopedics*. Published online 2013. doi:10.1016/j.ajodo.2013.07.011
20. Elnagar MH, Elshourbagy E, Ghobashy S, Khedr M, Evans CA. Comparative evaluation of 2 skeletally anchored maxillary protraction protocols. *Am J Orthod Dentofacial Orthop*. 2016;150(5):751-762. doi:10.1016/j.ajodo.2016.04.025
21. De Clerck H, Cevidanes L, Baccetti T. Dentofacial effects of bone-anchored maxillary protraction: A controlled study of consecutively treated Class III patients. *American Journal of Orthodontics and Dentofacial Orthopedics*. Published online 2010. doi:10.1016/j.ajodo.2009.10.037
22. Zhang W, Qu HC, Yu M, Zhang Y. The effects of maxillary protraction with or without rapid maxillary expansion and age factors in treating Class III malocclusion: A meta-Analysis. *PLoS One*. Published online 2015. doi:10.1371/journal.pone.0130096
23. Ngan P, Yiu C, Hu A, Hagg U, Wei SH, Gunel E. Cephalometric and occlusal changes following maxillary expansion and protraction. *Eur J Orthod*. 1998;20(3):237-254.
24. Nartallo-Turley PE, Turley PK. Cephalometric effects of combined palatal expansion and facemask therapy on Class III malocclusion. *Angle Orthod*. 1998;68(3):217-224. doi:10.1043/0003-3219(1998)068<0217:CEOCPE>2.3.CO;2
25. Vaughn GA, Mason B, Moon HB, Turley PK. The effects of maxillary protraction therapy with or without rapid palatal expansion: a prospective, randomized clinical trial. *Am J Orthod Dentofacial Orthop*. 2005;128(3):299-309. doi:10.1016/j.ajodo.2005.04.030
26. Macdonald KE, Kapust AJ, Turley PK. Cephalometric changes after the correction of class III malocclusion with maxillary expansion/facemask therapy. *Am J Orthod Dentofacial Orthop*. 1999;116(1):13-24. doi:10.1016/S0889-5406(99)70298-2
27. Cornelis MA, Tepedino M, Riis NDV, Niu X, Cattaneo PM. Treatment effect of bone-Anchored maxillary protraction in growing patients compared to controls: A systematic review with meta-Analysis. *Eur J Orthod*. 2021;43(1):51-68. doi:10.1093/ejo/cjaa016
28. Yepes E, Quintero P, Rueda ZV, Pedroza A. Optimal force for maxillary protraction facemask therapy in the early treatment of class III malocclusion. *Eur J Orthod*. 2014;36(5):586-594. doi:10.1093/ejo/cjt091
29. Van Hevele J, Nout E, Claeys T, Meyns J, Scheerlinck J, Politis C. Bone-anchored maxillary protraction to correct a class III skeletal relationship: A multicenter retrospective analysis of 218 patients. *Journal of Cranio-Maxillofacial Surgery*. 2018;46(10):1800-1806. doi:10.1016/j.jcms.2018.07.007
30. Meyns J, Brasil DM, Mazzi-Chaves JF, Politis C, Jacobs R. The clinical outcome of skeletal anchorage in interceptive treatment (in growing patients) for class III malocclusion. *Int J Oral Maxillofac Surg*. 2018;47(8):1003-1010. doi:10.1016/j.ijom.2018.04.011
31. Owens D, Watkinson S, Harrison JE, Turner S, Worthington H V. Orthodontic treatment for prominent lower front teeth (Class III malocclusion) in children (Review). *Cochrane Database of Systematic Reviews*. 2024;2024(4). doi:10.1002/14651858.CD003451.pub2

32. Wilmes B, Ludwig B, Katyal V, Nienkemper M, Rein A, Drescher D. The Hybrid Hyrax Distalizer, a new all-in-one appliance for rapid palatal expansion, early class III treatment and upper molar distalization. *J Orthod*. 2014;41(sup1):s47-s53. doi:10.1179/1465313314Y.0000000107
33. Ergul T, Gulec A. Comparison of the effectiveness of skeletal and tooth-borne protraction methods with or without alternate rapid maxillary expansion and constriction protocol in patients with Class III malocclusion. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2024;article in. doi:10.1016/j.ajodo.2024.10.010
34. Kim JH, Viana M a, Graber TM, Omerza FF, BeGole E a. The effectiveness of protraction face mask therapy: a meta-analysis. *Am J Orthod Dentofacial Orthop*. 1999;115(6):675-685. doi:10.1016/S0889-5406(99)70294-5
35. Foersch M, Jacobs C, Wriedt S, Hechtner M, Wehrbein H. Effectiveness of maxillary protraction using facemask with or without maxillary expansion: a systematic review and meta-analysis. *Clin Oral Investig*. 2015;19(6):1181-1192. doi:10.1007/s00784-015-1478-4
36. Masucci C, Franchi L, Giuntini V, Defraia E. Short-term effects of a modified Alt-RAMEC protocol for early treatment of Class III malocclusion: A controlled study. *Orthod Craniofac Res*. 2014;17(4):259-269. doi:10.1111/ocr.12051
37. Pithon MM, De N, Santos L, et al. Is alternate rapid maxillary expansion and constriction an effective protocol in the treatment of Class III malocclusion? A systematic review Is alternate rapid maxillary expansion and constriction protocol effective in the treatment of Class III maloc- c. *Dental Press J Orthod Dental Press J Orthod Dental Press J Orthod*. 2016;212121(666):34-4234. doi:10.1590/2177-6709.21.6.034-042.oar
38. Wu Z, Zhang X, Li Z, et al. A Bayesian network meta-analysis of orthopaedic treatment in Class III malocclusion: Maxillary protraction with skeletal anchorage or a rapid maxillary expander. *Orthod Craniofac Res*. 2020;23(1):1-15. doi:10.1111/ocr.12339
39. Wilmes B, Nienkemper M, Drescher D. Application and effectiveness of a mini-implant- and tooth-borne rapid palatal expansion device: the hybrid hyrax. *World J Orthod*. 2010;11(4):323-330. Accessed July 17, 2017. http://www.ncbi.nlm.nih.gov/pubmed/21490997
40. Wilmes B, Ngan P, Liou EJW, Franchi L, Drescher D. Early class III facemask treatment with the hybrid hyrax and Alt-RAMEC protocol. *J Clin Orthod*. 2014;48(2):84-93. Accessed July 17, 2017. http://www.ncbi.nlm.nih.gov/pubmed/24763681
41. Wilmes B, Nienkemper M, Ludwig B, Kau CH, Drescher D. Early Class III treatment with a hybrid hyrax-mentoplate combination. *J Clin Orthod*. 2011;(45):15–21. http://scholar.google.com/scholar?cluster=5963984962837880841&hl=en&oi=scholarr%5Cnhttp://www.researchgate.net/profile/Benedict_Wilmes/publication/51602783_Early_Class_III_treatment_with_a_hybrid_hyrax-mentoplate_combination/links/00b4952de81c6266f6000000
42. Katyal V, Wilmes B, Nienkemper M, Darendeliler MA, Sampson W, Drescher D. The efficacy of Hybrid Hyrax-Mentoplate combination in early Class III treatment: a novel approach and pilot study. *Aust Orthod J*. 2016;32(1):88-96. http://www.ncbi.nlm.nih.gov/pubmed/27468596
43. Hu S, An K, Peng Y. Comparative efficacy of the bone-anchored maxillary protraction protocols for orthopaedic treatment in skeletal Class III malocclusion: A Bayesian network meta-analysis. *Orthod Craniofac Res*. 2022;25(2):243-250. doi:10.1111/ocr.12532
44. YILDIRIM G, OZBİLEN EO, ÖZDEMİR F. Retrospective 3-dimensional Evaluation of Skeletal and Dental Structures Following Treatment with Hybrid Hyrax-Mentonplate with Class III Elastics in Class III Patients with Vertical Growth Pattern: A Pilot Study. *European Journal of Research in*

Dentistry. 2023;Cilt:7 Say(Cilt:7 Sayı:2):78-87. doi:10.29228/erd.49
45. Willmann JH, Nienkemper M, Tarraf NE, Wilmes B, Drescher D. Early Class III treatment with Hybrid-Hyrax – Facemask in comparison to Hybrid-Hyrax-Mentoplate – skeletal and dental outcomes. *Prog Orthod*. 2018;19(1):0-7. doi:10.1186/s40510-018-0239-8
46. Lin Y, Guo R, Hou L, Fu Z, Li W. Stability of maxillary protraction therapy in children with Class III malocclusion: a systematic review and meta-analysis. *Clin Oral Investig*. 2018;22(7):2639-2652. doi:10.1007/s00784-018-2363-8
47. Liou EJW, Tsai WC. A new protocol for maxillary protraction in cleft patients: Repetitive weekly protocol of alternate rapid maxillary expansions and constrictions. *Cleft Palate-Craniofacial Journal*. 2005;42(2):121-127. doi:10.1597/03-107.1
48. Miranda F, Cunha Bastos JC da, Magno dos Santos A, Janson G, Pereira Lauris JR, Garib D. Dentoskeletal comparison of miniscrew-anchored maxillary protraction with hybrid and conventional hyrax expanders: A randomized clinical trial. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2021;160(6):774-783. doi:10.1016/j.ajodo.2021.02.017
49. Ngan P, Wilmes B, Drescher D, Martin C, Weaver B, Gunel E. Comparison of two maxillary protraction protocols: tooth-borne versus bone-anchored protraction facemask treatment. *Prog Orthod*. 2015;16(1):26. doi:10.1186/s40510-015-0096-7
50. Alzoubi EE, Camilleri S, Al Muzian M, Attard N. The effect of tooth borne versus skeletally anchored Alt-RAMEC protocol in early treatment of Class III malocclusion: a single-centre randomized clinical trial. *Eur J Orthod*. 2023;45(5):517-527. doi:10.1093/ejo/cjad018
51. Mandall N, Aleid W, Cousley R, et al. The effectiveness of bone anchored maxillary protraction (BAMP) in the management of class III skeletal malocclusion in children aged 11–14 years compared with an untreated control group: A multicentre two-arm parallel randomised controlled trial. *J Orthod*. Published online 2024. doi:10.1177/14653125241255139
52. Miranda F, Garib D, Silva I, et al. Maxillary protraction anchored on miniplates versus miniscrews: three-dimensional dentoskeletal comparison. *Eur J Orthod*. 2024;47(1). doi:10.1093/ejo/cjae071
53. Gandedkar NH, Liou EJW. The immediate effect of alternate rapid maxillary expansions and constrictions on the alveolus: a retrospective cone beam computed tomography study. *Prog Orthod*. 2018;19(1):1-7. doi:10.1186/s40510-018-0237-x
54. Dehesa-Santos A, Iber-Diaz P, Iglesias-Linares A. Genetic factors contributing to skeletal class III malocclusion: a systematic review and meta-analysis. *Clin Oral Investig*. 2021;25(4):1587-1612. doi:10.1007/s00784-020-03731-5

SUPPLEMENTARY MATERIAL

Supplementary material 1: Details randomization sequence

Supplementary material 2: Facemask values

Supplementary material 3: Mentoplate values

S1: details randomization sequence

nr	date of enrollment	T0 baseline-scan	T1 one-year scan	T2 five-year scan	F / M	type of treatment	T0-T1 (months)	T0-T2 (months)
1	16/12/2016	14/02/2017	10/04/2018	8/02/2023	M	MP	13	71
2	16/12/2016	2/05/2017	27/02/2018	21/10/2022	F	MP	9	65
3	19/12/2016	28/02/2017	27/02/2018	21/10/2022	F	FM	11	67
4	21/12/2016	14/02/2017	21/02/2018	/	F	MP	12	/
5	21/12/2016	21/03/2017	21/02/2018	21/10/2022	M	MP	11	67
6	17/01/2017	21/03/2017	2/03/2018	21/10/2022	M	MP	11	67
7	24/01/2017	24/02/2017	21/02/2018	26/10/2022	M	FM	11	68
8	7/03/2017	4/04/2017	2/03/2018	15/03/2023	F	FM	10	71
9	15/03/2017	27/06/2017	22/06/2018	8/02/2023	F	MP	11	67
10	21/03/2017	6/10/2017	26/03/2019	9/11/2022	F	FM	17	61
11	28/03/2017	20/06/2017	22/06/2018	26/10/2022	F	MP	12	64
12	31/03/2017	5/05/2017	3/07/2018	9/11/2022	M	FM	13	66
13	31/03/2017	5/05/2017	3/07/2018	9/11/2022	F	FM	13	66
14	9/05/2017	14/11/2017	30/11/2018	8/02/2023	F	MP	12	62
15	9/08/2017	12/09/2017	17/07/2018	26/10/2022	M	MP	10	61
16	22/09/2017	27/11/2017	22/01/2019	1/02/2024	F	MP	13	74
17	26/09/2017	4/12/2017	/	/	F	MP	/	/
18	2/10/2017	18/10/2017	15/01/2019	15/03/2023	M	MP	14	64
19	17/10/2017	28/11/2017	22/01/2019	4/09/2023	M	FM	13	69
20	18/10/2017	21/11/2017	22/01/2019	9/11/2022	F	FM	14	59
21	24/10/2017	27/11/2017	15/01/2019	15/03/2023	M	MP	13	63
22	9/01/2018	27/02/2018	12/03/2019	/	M	FM	12	/
23	30/01/2018	2/03/2018	13/03/2019	/	M	FM	12	/
24	2/03/2018	2/03/2018	29/01/2019	4/09/2023	M	FM	10	66
25	1/06/2018	12/06/2018	14/05/2019	8/02/2023	F	MP	11	55
26	8/06/2018	8/06/2018	11/06/2019	30/08/2023	F	FM	12	62
27	27/06/2018	27/06/2018	25/06/2019	20/12/2023	M	FM	11	65
28	7/09/2018	19/09/2018	7/08/2019	26/10/2022	M	FM	10	49
						Mean	12,00	64,54
						SD	1,59	5,21

S2: Facemask values

		Sagittal				Vertical				Dental			
		SNA°	SNB°	ANB°	Wits	SNL-ML°	SNL-NL°	NL-ML°	PFH/AFH	U1 -SN	U1-FH	U1 -NL	IMPA
FM1	T0	80,2	80,6	-0,4	-3	30,5	9,1	21,4	67	104,7	116,9	110,8	88,7
	T1	82,3	79,7	2,6	1	30,7	7	23,6	67	104,9	117	110,3	86,8
	T2	82,5	80,4	2,1	1	27,4	11,2	16,2	70	115	129,2	124,5	96,4
FM2	T0	80,8	79,6	1,2	-4	30	11,8	18,2	69	94,2	105,3	103	79,4
	T1	82,7	79	3,7	-2	29,8	6,8	23	69	91,9	103,1	100,8	79,5
	T2	81,9	80	2	-3	30,4	9,9	20,4	70	97,8	112,2	106,5	91,1
FM3	T0	76,2	81,8	-5,6	-9	24,8	1,6	23,2	73	118,5	131,9	120,4	95,6
	T1	81,8	80,8	1	-3	24,5	-0,3	24,9	74	108,4	123,1	108,7	94,4
	T2	83	81	2	-1	22,9	3	19,9	76	113,5	123	114	106,9
FM4	T0	80,9	80,4	0,4	-5	33,5	2,2	31,3	66	103,5	113	106,5	91,9
	T1	85,7	80,1	5,6	1	34,8	5,2	29,6	65	97,5	112,8	103,7	91,7
	T2	85,5	81,7	3,7	-2	31,3	0,5	30,9	70	114,8	123	118,2	103,5
FM5	T0	77,8	77,5	0,3	-5	31,8	7,7	24,1	65	110,9	120,8	117,2	97,8
	T1	76,7	74,4	2,3	-1	33,7	5,9	27,8	64	103,9	115,4	109,7	96,3
	T2	76,4	77,4	-1	-4	30,5	4,3	26,3	69	107,8	119,3	113	98
FM6	T0	79,5	78,9	0,6	-7	37,5	13	24,5	60	104,4	122,2	119,3	90,5
	T1	81,1	80,7	0,4	-4	35,6	10,4	25,2	62	112,8	128,9	124,2	78
	T2	80,8	83	-2,2	-7	31,4	11,2	20,2	66	119,6	135,9	132,4	89,4
FM7	T0	77,8	81	-3,2	-7	29,6	0,9	28,7	65	112,3	120,9	114,5	86,8
	T1	77,2	78,6	-1,4	-3	32,3	4,3	28	64	98,8	108,3	101,8	87,7
	T2	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

S2: Facemask values (continued)

		Sagittal				Vertical				Dental			
		SNA°	SNB°	ANB°	Wits	SNL-ML°	SNL-NL°	NL-ML°	PFH/AFH	U1 -SN	U1-FH	U1 -NL	IMPA
	T0	82,1	81,5	0,5	-6	31,3	4,5	26,8	65	97,6	109,5	105,8	87
FM8	T1	83	81,1	1,9	-4	31	3,7	27,4	65	97,5	109	103,1	83,8
	T2	85	86,8	-1,8	-5	21,7	-0,4	22,1	74	112,3	122,1	117,5	91,4
	T0	76,5	76	0,6	-6	41,6	6,3	35,3	59	101,1	115,9	110,4	93,4
FM9	T1	83,4	75,8	7,6	3	40,3	6,5	33,8	59	99,6	113,6	107	93
	T2	82,2	76,8	5,4	0	38,6	5,2	33,4	61	104,9	119,9	110,1	94,3
	T0	78,3	78,8	-0,6	-7	34,8	8,8	25,9	64	101,9	120,2	115	97,7
FM10	T1	80,1	78,6	1,5	-5	36,9	12,2	24,8	61	98,5	116,2	111,2	92
	T2	82,4	77	5,4	0	37,1	12,8	24,3	63	110,6	128,6	124,9	98,9
	T0	82,6	83,4	-0,8	-6	32	5,7	26,3	63	108,1	121,7	114,6	84,1
FM11	T1	83,8	80,4	3,4	-1	34,2	6,8	27,4	60	107,7	121,7	112	74,1
	T2	80,7	80	0,7	-4	32,6	9,4	23,2	62	111,4	125,7	121,2	87,4
	T0	76,4	80,6	-4,2	-8	29,7	7,5	22,1	67	110,7	126,1	121,5	94,4
FM12	T1	81	80,6	0,5	-2	29,5	8,5	21	66	105,1	120,5	113,7	92,4
	T2	81,8	84,9	-3	-5	23,7	3,8	19,9	72	115,9	128,3	122	89
	T0	83,9	83,9	0	-4	25,7	6,9	18,8	72	103,5	114,8	109,1	89,2
FM13	T1	86,3	83,3	3	-1	25,6	8,1	17,5	72	101,6	114,4	107	93,1
	T2	NA	NA	NA		NA	NA	NA	NA	NA	NA	NA	NA
	T0	78,8	79,1	-0,3	-3	31,1	4,9	26,2	65	106	118,7	114	89,3
FM14	T1	79,9	79,7	0,2	-2	31,7	6,3	25,4	64	110,8	122,9	117,7	88,6
	T2	78,7	80,4	-1,7	-3	29,3	7,3	22	66	113,2	125,2	119,3	84,3

S3: Mentoplate values

		Sagittal				Vertical				Dental			
		SNA°	SNB°	ANB°	Wits	SNL-ML°	SNL-NL°	NL-ML°	PFH/AFH	U1-SN	U1-FH	U1-NL	IMPA
MP1	T0	76,1	76,1	0	-5	33,6	7,7	25,9	64	87,2	100	98,4	89,9
	T1	74,9	74,2	0,7	-4,7	35,1	8,6	26,5	62	89,5	102,5	101,7	91,6
	T2	75,6	76,3	-0,8	-3	30,2	8,8	21,4	68	94,6	105,5	107,2	95,5
MP2	T0	70,3	68,9	1,4	-10	51,8	11,4	40,4	52	92,8	107,7	106,5	89,8
	T1	70,8	67,4	3,5	-4	48,5	19,8	28,7	55	97,8	114,2	116,5	84
	T2	68,4	67,9	0,5	-9	48,4	16,7	31,7	56	95,8	110,5	111,8	92,2
MP3	T0	80,8	80	0,9	-6	31,7	10,5	21,2	64	96,9	105,7	107,6	102,9
	T1	82,2	78,2	4,1	1	29,4	7,7	21,6	66	106,7	116,6	118	108,4
	T2	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
MP4	T0	80	80	0	-7	39,3	16,5	22,8	60	106,2	115,5	118,1	81,9
	T1	83,5	82	1,6	-8	37,1	12,6	24,5	62	108,3	117,8	121,9	89
	T2	83,2	81,8	1,5	-5	37,3	13,5	23,8	61	119,4	128,4	131,2	87,5
MP5	T0	72,9	72,5	0,5	-2	38,6	14,2	24,4	61	105,5	121,8	116,6	94,4
	T1	78,3	75,8	2,5	-1	34,6	10,7	23,9	63	109,8	121,9	120,7	95,6
	T2	76,2	75	1,2	-3	36,1	10	26,1	64	105,3	123,8	118,4	94,8
MP6	T0	80,1	81,3	-1,1	-5	31,9	3,5	28,4	62	114,3	126,9	120,6	102
	T1	82	80,6	1,4	-2	31,1	4,1	27	63	115,2	126,3	120,2	99,7
	T2	82	81,9	0,1	-6	30	7,6	22,5	66	114,4	126,6	122,3	104
MP7	T0	79,6	78,9	0,7	-4	36,3	7,3	29	63	103,7	112,9	113,5	81,6
	T1	81,2	77,5	3,7	-2	35,7	9,3	26,3	64	100,7	109,1	112,1	90,7
	T2	81,2	77,6	3,6	1	35,1	7,4	27,7	64	113,4	125,8	122,8	100,7

S3: Mentoplate values (continued)

		Sagittal				Vertical				Dental			
		SNA°	SNB°	ANB°	Wits	SNL-ML°	SNL-NL°	NL-ML°	PFH/AFH	U1 -SN	U1-FH	U1 -NL	IMPA
MP8	T0	79,3	80	-0,8	-2	29,7	9,9	19,8	67	122	128,2	129	101,1
	T1	81,3	78,7	2,6	0	30,9	4,8	26,1	66	111,1	120,6	117,6	111,5
	T2	82,3	83,7	-1,4	-6	28,2	7,1	21,1	69	123,4	131	129,8	93,5
MP9	T0	79,2	80	-0,8	-4	27,1	5,8	21,2	69	109,6	123,1	117,3	92
	T1	81,4	78,2	3,2	0	28,7	4,8	23,9	68	109,5	124,5	116,4	95
	T2	82,2	81,5	0,7	-4	27,7	7,5	20,2	70	109	123,5	114,5	91,8
MP10	T0	77,3	79,4	-2,1	-7	36	8,3	27,6	63	95,4	103,6	113,8	84,7
	T1	76,4	78,3	-1,9	-7	37,3	6,8	30,5	62	109,1	124,1	120,7	84,1
	T2	80,4	78,6	1,8	-5	37	14,2	22,8	63	111,1	126	126,9	94,2
MP11	T0	79,1	83,2	-4,1	-8	32,8	12,2	20,6	63	105,9	118,7	121,2	84,6
	T1	84,1	83,2	0,9	-4	33,3	8,7	24,6	62	107,2	120,7	116,3	93,7
	T2	85,9	85,2	0,7	-6	32,6	10	22,6	64	115,5	131,2	130,5	85,7
MP12	T0	83,3	84,7	-1,4	-8	34,9	1,3	33,6	64	109,1	121,4	114,6	92,9
	T1	85,8	83,2	2,5	-2	36,5	2,2	34,2	62	106,5	116,3	110,3	84,4
	T2	87,4	84,9	2,4	-1	30	1,6	28,4	68	105,2	117,1	107,8	85,7
MP13	T0	80,9	81,2	-0,3	-5	32	4,8	27,2	67	104,2	118,6	110,9	90,4
	T1	86,5	82,6	3,9	0	31,8	2,4	29,3	67	99,2	109,5	101,8	90,1
	T2	87,7	84,3	3,4	-3	32,2	3.3	24,6	69	101,8	112,2	103,9	89,2

CHAPTER 6

Overall 3-Dimensional assessment

This chapter is based on the following manuscript.

Meyns J., Jindanil T., Shujaat S., Politis C., Jacobs R. Long-term Three-dimensional Skeletal Effects of Hybrid Hyrax with Facemask versus Mentoplate in Growing Class III Patients: A Randomized Controlled Trial.

Progress in Orthodontics, 26 (14) April 2025

ABSTRACT

Background:

Early intervention in Class III malocclusion aims to prevent the need for surgery in adulthood by enhancing upper jaw growth while limiting lower jaw development. Although traditional facemask treatment remain common, bone-anchored devices are increasingly used, claiming better skeletal control and patient compliance. However, strong evidence supporting these advantages is limited.

Methods:

Single-center, parallel-group, randomized controlled trial with 1:1 allocation ratio.

Participants: 28 growing Class III patients (mean age 9.7 ± 1.3 years) in mixed dentition with skeletal class III malocclusion.

Interventions: Patients were randomly assigned to either hybrid hyrax with facemask (HH+FM, n=14) or hybrid hyrax with mentoplate (HH+MP, n=14). All received Alt-RAMEC protocol expansion. FM group used 360-400g/side elastic traction 12-14 hours daily; MP group used 185g/side continuous traction. *Objective:* To compare 5-year three-dimensional (3D) skeletal effects between HH+FM and HH+MP protocols.

Outcome: Primary outcome was 3D volumetric changes of upper and lower jaw at 1 year (T1) and 5 years (T2) post-treatment, measured using low-dose CT scans.

Randomization: 28 patients were allocated to either treatment-protocols using sequentially numbered opaque, sealed envelopes. The randomization sequence was generated with a 1:1 allocation ratio.

Blinding: Due to the nature of the trial, the operator and children could not be blinded to the treatment allocation. However, blinding was used when assessing the outcomes.

Results:

Follow-up: one patient was lost at the one-year follow-up and an additional three patients were lost at the 5-year-follow-up.

Outcomes: At T2 (5 years), maxillary advancement was identical between both groups (0.85 mm ± 0.5). Mandibular growth control showed minimal difference (FM: -0.01 mm ± 0.24; MP: 0.10 mm ± 0.33). No significant differences were found

between groups for any skeletal measurements ($p>0.05$). Male patients showed lager mandibular changes both signed ($p <0.03$) and unsigned ($p <0.01$).
Harms: minor harms were encountered with the anchor hooks (fracture or mucosal irritation), however none led to treatment cessation.

<u>Conclusions:</u>

Both protocols demonstrated comparable long-term skeletal effects in Class III correction. Treatment choice should be based on individual patient factors rather than assumed mechanical advantages.

<u>Trial Registration:</u>

www.ClinicalTrials.gov (ID: NCT02711111)

Funding: none

INTRODUCTION

Background

Class III malocclusion affects approximately 0 to 26 % of the population [1] and can significantly impact both function and aesthetics. While early intervention is often recommended, clinicians face a critical choice: should they use traditional facemask (FM) therapy [2] or newer bone-anchored techniques [3] ? Despite the growing popularity of bone-anchored treatments, no long-term randomized trials have compared their effectiveness to traditional approaches [4–6]. While FM therapy is the traditional treatment approach with well-documented results, its long-term success is not guaranteed. Most Studies on interceptive class III treatment typically have limited long-term follow-up data [4]. Treatment effects often diminish over time as patients continue to grow. Limited long-term studies indicate that 25-30% of patients may still require orthognathic surgery despite early intervention [7,8]. Additionally, traditional FM therapy can cause unwanted effects, including mandibular autorotation and dental compensations, primarily because forces are applied indirectly through the teeth [9]. To overcome the limitations of conventional FM therapy and address more severe class III deformities, various skeletal anchorage techniques, using screws and bone plates, have gained popularity and are used in conjunction with both intra- and extra-oral devices [10–24]. Despite the widespread use of skeletal anchorage devices for interceptive Class III treatment, there is ongoing debate about their effectiveness compared to traditional FM treatment [4–6,12,25,26]. High-quality comparative evidence, particularly randomized controlled trials (RCTs), is scarce in this field [4–6,26] . While skeletal anchorage techniques offer advantages, they are not without potential drawbacks, such as the need for invasive procedures and potential instability of anchoring devices [27,28].

The hybrid hyrax (HH) device [29] utilizes two mini-implants in the anterior palate to provide skeletal anchorage for maxillary protraction while also performing rapid maxillary expansion. Although the effectiveness of rapid palatal expansion (RPE) in enhancing maxillary protraction, remains controversial [30–32], HH therapy is gaining popularity due to its low invasiveness compared to traditional bone-anchors in the upper jaw. However, its effectiveness when combined with various protraction methods, such as FM and mentoplate (MP), has not been directly compared in a controlled study. Moreover, no comparative three-dimensional (3D) data exists quantifying the skeletal changes following HH+FM and HH+MP treatment protocols [4]. The potential advantages of MP over FM in terms of skeletal impact and patient compliance have been hypothesized, but not empirically verified in a comparative study [25].

Objective

This prospective RCT aimed to compare the 5-year long-term 3D skeletal effects of HH+FM and HH+ MP treatment protocols in growing class III patients using low dose computed tomography (CT) scans.

METHODS

Trial design

A single-center 2-arm parallel randomized controlled trial with 1:1 allocation ratio

Participants

This study examined patients with Class III skeletal malocclusion that were referred to our hospital by their orthodontist. Enrollment took place from December 2016 to September 2018 (complete data available in Supplementary File 1). All participants were in mixed dentition with anterior crossbite or an end-to-end incisor relationship and Class III molar relationship at the start of treatment. Patients were excluded if they had cleft/craniofacial syndromes, prior orthodontic/surgical treatment, significant skeletal asymmetry, or functional Class III malocclusion. No agenesis of a permanent central incisor was present in any patient. A single surgeon performed HH screw and MP placements, while three experienced orthodontists provided orthodontic care.

Interventions

Palatal expansion by HH

In all patients, 2 self-drilling mini-screws (2 mm in diameter and 9 mm long, Benefit miniscrews, PSM-medical solutions®, Gunningen, Germany) were inserted free-handed into the anterior palate around the third rugae. A HH device was constructed with an expansion screw (Forestadent®, Pforzheim Germany) and welded to bands.

These bands were then cemented to the first upper molars with a light cured cement (Band-Lok®, Reliance Orthodontic Products, Thorndale, USA) (Figure 6.1). The Alternate Rapid Maxillary Expansion and Constriction (Alt-RAMEC) protocol [33] was implemented, where the hyrax was activated by the patient's parents twice a day (0.25 mm per turn, two turns in morning and two turns at night) for 1 week, then it was deactivated twice a day (two turns in morning and two turns at night) for 1 week. This alternating activation and deactivation cycle was carried out three times. Subsequently, in the ensuing week, the maxilla was adjusted to the suitable transverse dimension.

FM group

In this group, FM therapy commenced concurrently with Alt-RAMEC. Elastics (American Orthodontics ®, Sjeboygan, USA) were connected from the hooks of the expander to the FM (Orthocomfort & Medical Distributors SL®, Barcelona, Spain), creating a downward and forward vector. This configuration produced orthopedic forces of 360 – 400 g per side (equivalent to 12.7 – 14.0 oz). The patients were instructed to use the device for 12 – 14 hours daily, primarily overnight, for the initial six months or until they achieved a positive overjet of at least 2 mm. For the following six months, the FM was to be worn only during sleep (Figure 6.1).

MP group

During general anesthesia, MP (PSM-medical solutions®, Gunningen, Germany) was inserted through a marginal gingival incision. The plate was bent and modified before fixation with 2 to 4 screws (KLS Martin®, Tuttlingen, Germany) (Figure 6.1). The patients were simultaneously given Alt-RAMEC and protraction elastics, generating orthopedic forces of 185 g per side (equivalent to 6 ½ oz). Elastic traction was initiated approximately two weeks after plate insertion, once the soft tissues had healed. Full force was applied immediately, without gradual buildup. The patients were instructed to wear it continuously, 24 hours a day, 7 days a week, including during meals. They were also advised to replace the elastics daily for the first six months or until a positive overjet of at least 2 mm was achieved. For the subsequent six months, the elastics were to be worn only during sleep.

Fixed appliances

Phase 1 consisted of protraction therapy alone, without fixed appliances, from baseline (T0) to one year (T1). In Phase 2, all patients received standard fixed orthodontic appliances (edgewise mechanics, MBT .022, Empower R, American Orthodontics ®). Both phases followed standardized treatment protocols. In three MP patients and one FM patient, four premolar extractions were required. Additionally, one FM patient underwent the extraction of two premolars in the lower jaw.

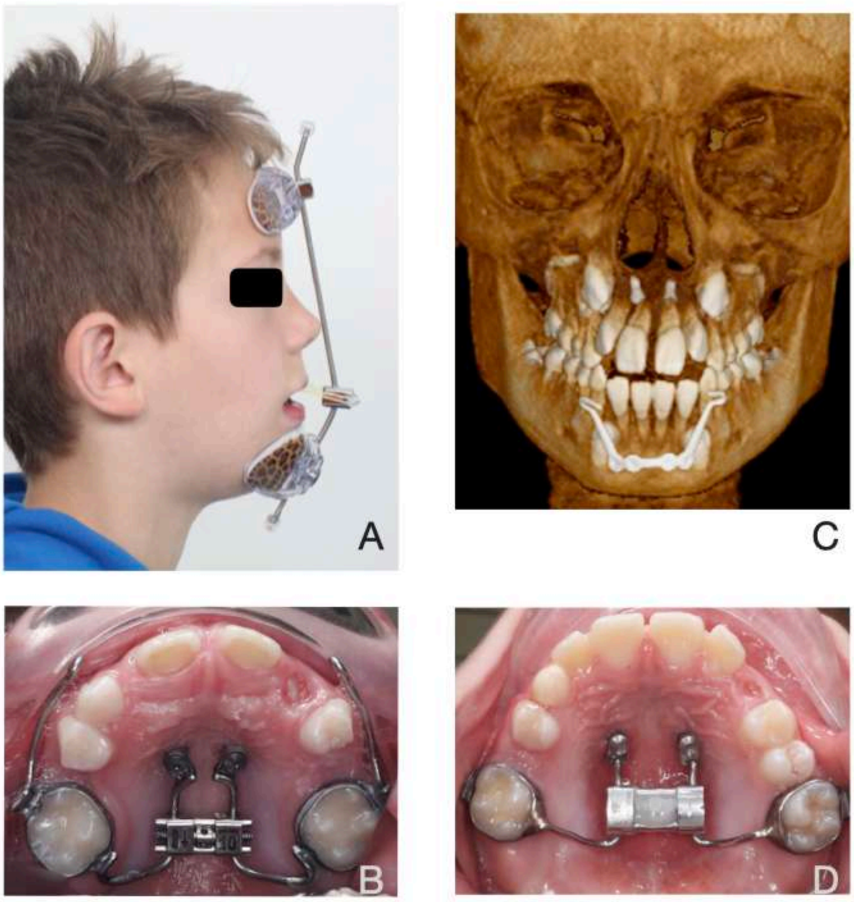


Figure 6.1:
A: extra-oral view Facemask (FM), B: Hybrid hyrax FM, C: Mentoplate (MP) secured between impacted canines, D: Hybrid hyrax MP

Outcomes

The primary outcomes were 3D volumetric changes of upper and lower jaw at T1 and T2 post treatment time-points.

Radiographic data acquisition

Low-dose CT scans were acquired by the same technician at three time points (T0, T1, and T2). All patients were positioned supine in the CT scanner, with a wax bite in centric relation placed between their teeth in first tooth contact. Subjects were given instructions to remain still, abstain from swallowing, and maintain normal breathing during the scan acquisition. Scans were performed using a Somatom Force dual-source dual-energy CT system (Siemens®, Erlangen, Germany) with the following parameters: - 0.6 mm slice thickness - 0.3 mm increment - 1.0 pitch - 200 x 200 mm field of view - 150 kVp tube voltage. CT scans delivered radiation doses of 0.095-0.257 mSv, similar to cone-beam CT (CBCT) levels. The CT system provided superior image quality and faster scanning times, reducing motion artifacts while maintaining low radiation exposure through automatic dose modulation.

3D skeletal analysis

The T0, T1 and T2 CT datasets were imported into Amira® software (version 2019.1, Thermo Fischer Scientific®, Merignac, France) in DICOM format. Volume rendering was applied to visualize the skeletal tissue. A rigid voxel-based registration using mutual information was performed to superimpose the T1 and T2 onto T0 datasets. The maxilla and mandible were separately registered using the anterior cranial base for the maxillary region and the anterior chin and internal symphysis for the mandible, as these regions are recognized as stable and reliable for voxel-based superimposition in growing patients [34–36]. The registered CT datasets were then imported into Virtual Patient Creator (version 2.2.0, September 2024, Relu ® BV, Leuven, Belgium), an online cloud-based platform that enables automatic segmentation of the maxillofacial anatomical structures. The anatomical segmentation, including both the maxillary and mandibular bones, was exported in Standard Tessellation Language (STL) format and refinement was performed in Mimics® software (version 20.0, Materialise®, Leuven, Belgium), if necessary. Teeth and surrounding alveolar bone were excluded from measurements to isolate true skeletal changes. The refined 3D surface models were imported in to 3-matic® software (version 14.0, Materialise®, Leuven, Belgium) for surface distance measurement between T0 and registered T1/ T2 maxilla and mandible. This allowed for the automatic calculation of the treatment effect, as mean difference between T0/T1, T0/T2 and T1/T2 images which was represented by a color-coded map. Figure 6.2 illustrates the flowchart outlining the methods, starting from CT registration to the final analysis. All measurements were performed by two independent operators (SS and TJ), and 10% of the data were analyzed twice to determine the inter- and intra-observer reliability.

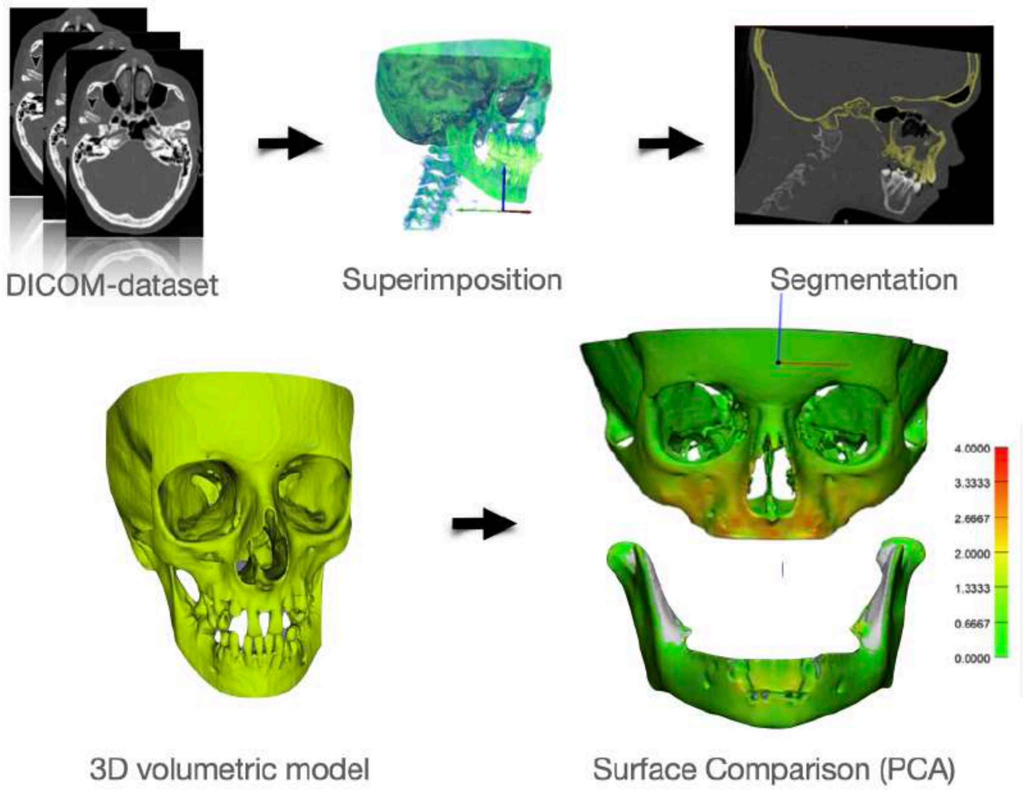


Figure 6.2: Flow-diagram 3D volumetric analysis:

i. Superimposition of T0/T1/T2 data-set in Amira® (maxilla superimposed on cranial base, mandible superimposed on internal symphyseal region)
ii. Segmentation in Mimics® generating 3D volumetric models (*stl)
iii. Surface comparison through Part Comparison Analysis (PCA) in 3-matic® (Teeth and surrounding alveolar bone are excluded)

Cephalometric analysis of baseline values

The assessment of Class III severity was conducted by evaluating the ANB angle and Wits' appraisal at the commencement of treatment. This evaluation was performed on two-dimensional (2D) cephalometric image, generated from the CT dataset, with Planmeca Romexis® software (version 6.3.0, Planmeca®, Helsinki, Finland), using an orthogonal method without magnification. Cephalometric analysis was done with the OnyxCeph® software (version 3.6, Image Instruments GmbH®, Chemnitz.

The skeletal maturation was assessed according to the cervical vertebral maturation method [37]. Two independent oral and maxillofacial surgery trainees analyzed 10% of the data twice to determine the inter- and intra-observer reliability.

Sample Size calculation

When this trial began in 2016, no comparative studies of these specific techniques existed. In 2010 Cevidanes et al. [11] conducted a controlled clinical trial comparing Bone Anchored Maxillary Protraction (BAMP) with Facemask and Rapid Maxillary Expansion (FM-RME), finding a mean Wits difference of 2.3 mm between groups. We pooled the standard deviations from both groups by first converting them to variances by squaring the standard deviations, then taking the average, and converting the average back to a standard deviation by taking the square root (resulting in a SD = 2,0). A sample size calculation was performed for a one-sided t-test with a significance level of 0.05 and a power of 80%. This resulted in a required sample size of 12 patients per group. R version 4.1.2 was used, with the TrialSize library to calculate the sample size. We slightly overrecruited to account for potential dropouts.

Randomisation

Sequence generation

The randomization sequence was generated with a 1:1 allocation ratio. (for complete data, supplementary material 1)

Allocation concealment

Sequentially numbered sealed, opaque envelopes.

Implementation

The envelopes containing the allocation sequence codes were given to the patient by an intermediary and opened sequentially at the time of enrollment, excluding the clinician from the process.

Blinding

Due to the nature of the trial, the operator and children could not be blinded to the treatment allocation. However, blinding was used when assessing the outcomes. This was achieved by pseudonymizing all patient data before and after treatment. The statistician analyzing the results was unaware of the group assignments.

Statistical methods

We used a Generalized Estimating Equation (GEE) model to assess treatment effects. The model analyzed differences between time points (T2-T0, T1-T0, and T2-T1), with measurements clustered by patient. This approach accounts for measurement error while incorporating all data points. The model included treatment group interactions across time points, along with covariates for patient age (in months), gender, and gonial angle. An identity link function was applied to handle normal responses, similar to linear regression but adjusted for clustered data. We specified an unstructured working correlation matrix and implemented the model using the geeglm function in R (version 4.4.1) from the geepack package. Reliability of cephalometric and 3D volumetric measurements was assessed using Intra-Class Correlation Coefficients (ICC) with 95% confidence intervals. Statistical significance was set at $p < 0.05$. Cephalometric measurements at baseline are described in mean with standard deviations. Unpaired two-sided samples t-test was employed for comparisons between the two groups.

RESULTS

Participants flow

A total of 28 patients were recruited, comprising of an equal number of males and females (n=14 each). One patient, initially assigned to the MP group, was later excluded due to non-cooperation leading to discontinuation of treatment. Three additional patients, two from the FM group and one from the MP group, were lost to follow-up before the 5-year time-point (Figure 6.3).

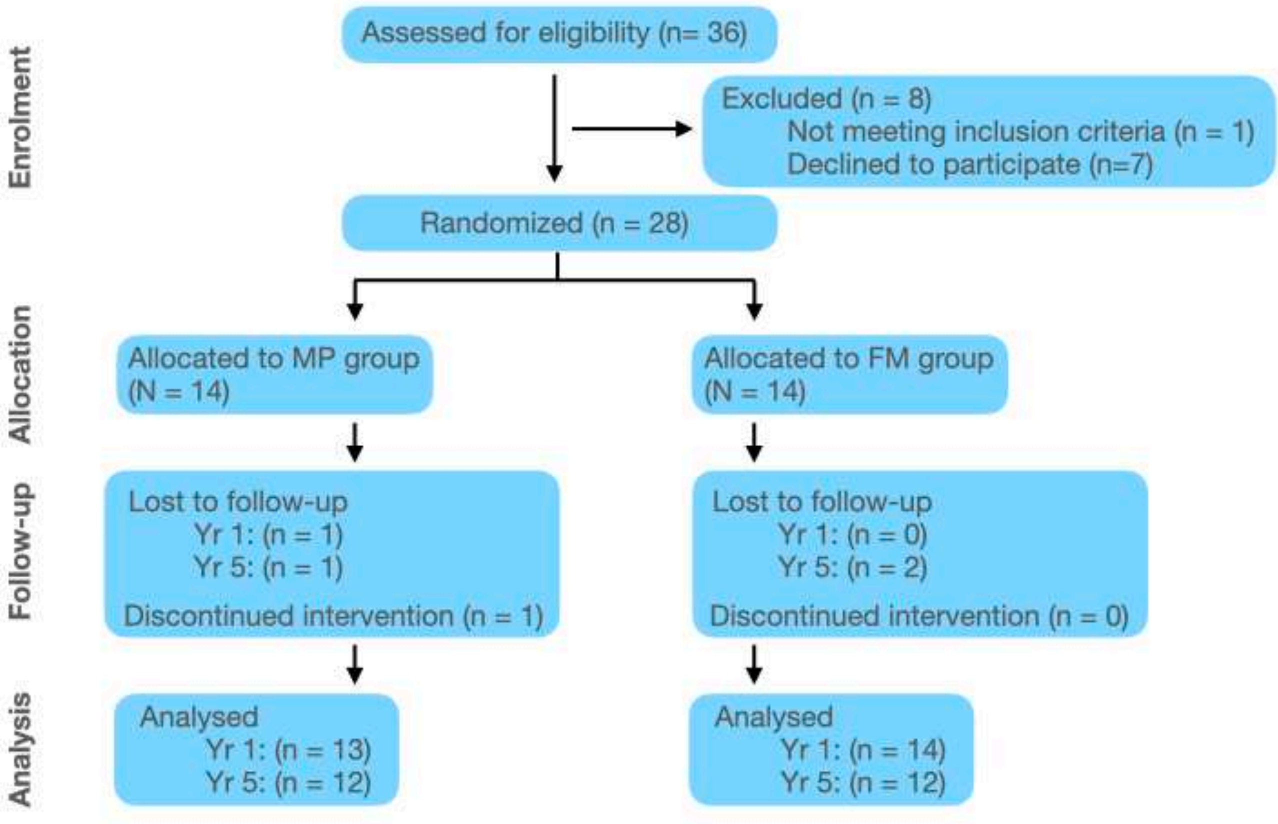


Figure 6.3: Participants flow

Recruitment

Patient recruitment occurred from December 2016 to September 2018. Scans were performed in three phases: initial scans (T0) from February 2017 to September 2018, first follow-up (T1) from February 2018 to August 2019, and second follow-up (T2) from October 2022 to February 2024. (supplementary material 1 for more details)

Baseline data

The study included 28 patients (14 of each gender, average age 9.7 years ± 1.3). Both treatment groups were matched for age and gender. All but one patient had reached cervical vertebral maturation stages 2 or 3. Both groups showed similar Class III malocclusion severity based on ANB and Wits measurements (Table 6.1).

Table 6.1: group characteristics at T0 (start treatment)

	Facemask Mean (SD)	**Mentoplate** Mean (SD)	p-value
Sagittal			
SNA °	79.41 (2.43)	78.38 (3.50)	0.38
SNB °	80.22 (2.14)	78.94 (4.25)	0.33
ANB °	-0.82 (2.03)	-0.55 (1.45)	0.69
Wits (mm)	-5.71 (1.82)	-5.62 (2.36)	0.90
F/M	7/7	7/7	
age (T0)	9 y, 6 mo	9 y, 7 mo	
follow-up (T2)	64 mo	65 mo	

F/M: Female/ Male; Follow-up (T2): mean follow-up time in months, p-value (unpaired two-sided samples t-test). Baseline comparisons are provided for descriptive purposes only, to confirm group equivalence following randomization, and should not be interpreted as inferential statistical analyses.

Numbers analyzed.

Twenty-eight patients (14 FM, 14 MP) underwent low dose CT at baseline (T0). At T1, 27 patients (14 FM, 13 MP) completed follow-up scans. By T2, 24 patients (12 FM, 12 MP) remained for analysis (Figure 6.3).

Outcomes and estimation

Both inter-observer (ICC: 0.95-0.98) and intra-observer (ICC: 0.93-0.98) measurements showed high reliability with no significant differences between observers. Mean follow-up time was 12 ± 1.59 months at T1 and 64.5 ± 5.21 months at T2 (Table 6.1). The skeletal changes are reported as both mean (signed) and absolute mean (unsigned) values. The 3D changes in maxillary and mandibular skeletal surfaces between the T0, T1 and T2 time points for both the FM and MP groups are shown in Table 6.2. A GEE model was fit to analyze the changes over time with type of treatment, age, gender and gonial angle as covariate. The difference in the FM group during active treatment period (T1-T0) is the reference group in the model (Table 6.3, Figure 6.4, and Figure 6.5). The signed mean values show both direction and magnitude of skeletal changes. A positive sign indicates anterior movement, while a negative sign shows posterior movement across three time periods (T0-T1, T0-T2, and T1-T2). Meanwhile, the unsigned mean values (absolute values) measure only the magnitude of changes, regardless of direction. Together, these measurements provide both qualitative (directional) and quantitative (magnitude) insights into skeletal changes.

When controlling for sex, age and gonial angle, both FM and MP treatments demonstrated similar effectiveness in maxillary advancement (signed values), with MP achieving slightly less advancement than FM (0.10 mm less at T1, $p=0.18$). Initial forward movement was minimal (0.21–0.28 mm) but increased to 0.85 mm in both groups by the end of treatment. Notably, changes during follow-up (T2–T1) were 0.54 mm greater than those observed during active treatment (T1–T0, $p < 0.01$)). Total maxillary changes (unsigned values) increased from 0.9 mm initially to 1.4 mm at treatment completion, with no significant differences between groups (MP group exhibited 0.11 mm smaller changes at T1, $p=0.25$ during active treatment).

Both treatments effectively controlled mandibular growth. Initial forward movement (mean signed values) was minimal in both groups (FM: 0.03 mm; MP: 0.07 mm), with MP showing slightly smaller changes (0.02 mm less, p=0.81) during active treatment. By the end of treatment, the FM group exhibited slight backward movement (-0.01 mm), while the MP group remained stable (0.1 mm). Final mandibular changes (unsigned values) were comparable between groups (p=0.22). Signed mandibular changes during active treatment (T1-T0) were comparable to the signed changes observed during follow-up (T2-T1), p = 0.63. The unsigned changes during active treatment (T1-T0) were significantly smaller (0.47 mm) then during follow-up (T2-T1) (p <0.01). Males experienced larger mandibular changes than females across both groups, with 0.28 mm greater absolute changes and 0.17 mm greater directional changes (p<0.01 and p=0.03, respectively). Additionally, patients with larger gonial angles demonstrated significantly greater mandibular volume changes. This effect was statistically significant in both signed (p=0.05) and unsigned measurements (p=0.01) (Table 6.3) (Supplementary material 2 for complete data).

Table 6.2: 3D volumetric changes

	T0-T1		T0-T2		T1-T2	
S mean	Facemask	Mentoplate	Facemask	Mentoplate	Facemask	Mentoplate
Mx	0.28 (0.20)	0.21 (0.17)	0.85 (0.50)	0.85 (0.51)	0.82 (0.69)	0.59 (0.45)
Md	0.03 (0.21)	0.07 (0.09)	-0.01 (0.24)	0.10 (0.33)	0.06 (0.27)	0.10 (0.32)
US mean	Facemask	Mentoplate	Facemask	Mentoplate	Facemask	Mentoplate
Mx	0.91 (0.23)	0.84 (0.30)	1.41 (0.43)	1.44 (0.44)	1.40 (0.57)	1.28 (0.36)
Md	0.66 (0.28)	0.57 (0.16)	1.19 (0.24)	1.30 (0.36)	1.11 (0.31)	1.22 (0.42)
% forward growth	Facemask	Mentoplate	Facemask	Mentoplate	Facemask	Mentoplate
Mx	0.30	0.25	0.60	0.59	0.58	0.46
Md	0.05	0.12	-0.01	0.08	0.05	0.08

S mean: Signed mean; US mean: Unsigned mean; Mx: Maxilla; Md: Mandible; mean (Standard Deviation); % forward growth: Signed mean/ Unsigned mean.

Table 6.3: GEE-model

	Mx Signed				Mx Unsigned				Md Signed				Md Unsigned			
co-variate	**Estimate**	**Std.err**	**95% CI**	**p-value**	**Estimate**	**Std.err**	**95% CI**	**p-value**	**Estimate**	**Std.err**	**95% CI**	**p-value**	**Estimate**	**Std.err**	**95% CI**	**p-value**
Intercept	-0.32	1.26	-2.78 /2.14	0.80	-0.68	1.61	-3.84/ 2.49	0.67	-2.47	1.08	-4.58 / -0.36	**0.02**	-1.13	0.88	-2.85 / 0.59	0.20
Mentoplate: T1-T0	-0.10	0.08	-0.25 / 0.05	0.18	-0.11	0.10	-0.30/0.08	0.25	-0.02	0.08	-0.18 / 0.14	0.81	-0.15	0.12	-0.38 / 0.09	0.22
T2-T1 (FM + MP)	0.54	0.17	0.22 / 0.86	**<0.01**	0.55	0.12	0.31 / 0.78	**<0.01**	-0.04	0.08	-0.19 / 0.11	0.63	0.47	0.13	0.22 / 0.72	**<0.01**
T2-T0 (FM + MP)	0.58	0.13	0.32/0.83	**<0.01**	0.53	0.12	0.30 / 0.76	**<0.01**	0.04	0.10	-0.15 / 0.23	0.67	0.55	0.11	0.33 / 0.77	**<0.01**
Male	-0.02	0.11	-0.24 / 0.19	0.84	0.08	0.12	-0.17 / 0.32	0.54	0.17	0.08	0.01 / 0.33	**0.03**	0.28	0.06	0.16 / 0.39	**<0.01**
Age (months)	-0.003	0.003	-0.01 / 0.002	0.24	-0.002	0.003	-0.01 / 0.004	0.54	0.004	0.002	0.001 / 0.009	**0.02**	-0.002	0.002	-0.006 / 0.002	0.36
Gonial angle	0.01	0.01	-0.01/0.03	0.35	0.01	0.01	-0.01 / 0.03	0.17	0.02	0.01	<0.01 / 0.03	**0.05**	0.02	0.01	0.004 / 0.03	**0.01**
Mentoplate:T2-T1	-0.16	0.21	-0.56/0.24	0.43	0.07	0.20	-0.32/ 0.46	0.73	0.07	0.12	.-0.16 / 0.30	0.54	0.18	0.18	-0.18 / 0.54	0.33
Mentoplate: T2-T0	0.06	0.22	-0.365 /0.48	0.80	-0.13	0.15	-0.42 / 0.16	0.37	-0.01	0.14	-0.28 / 0.27	0.96	0.19	0.15	-0.11 / 0.48	0.22

Mx: maxilla; Md: mandible; Std.err: standard error; 95%CI: Confidence Interval; FM: Facemask; MP: mentoplate.
Differences are described in mm, interaction effect needs to be calculated, with the difference in the FM group during active treatment period (T1-T0) as reference group. Eg: differences in changes in the MP group T2-T0 compared to the FM group T2-T0 = (difference mentoplate: T1-T0) + (difference Mentoplate: T2 -T0) = -0.10 + 0.06 = - 0.04

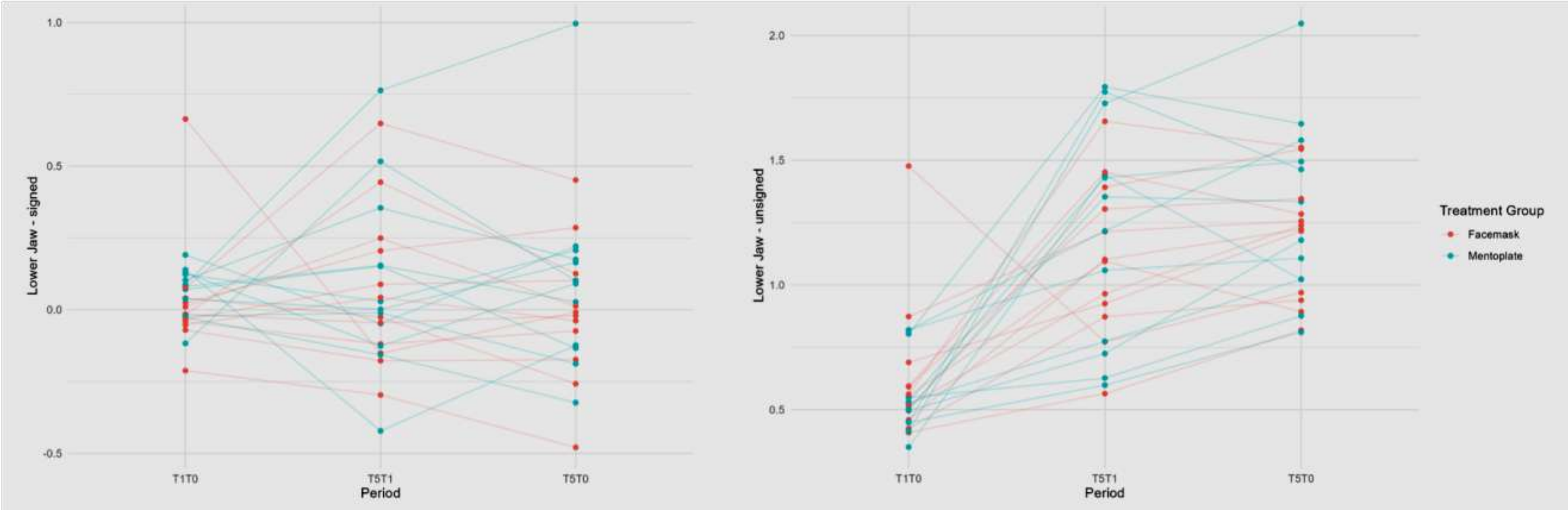


Figure 6.4: Scatter plot mandibular changes; T1T0: changes during active treatment (year 1); T5T1: changes during flow-up (year 1 – 5); T5T0: changes overall (start- year 5); Left: signed changes; right: unsigned changes.

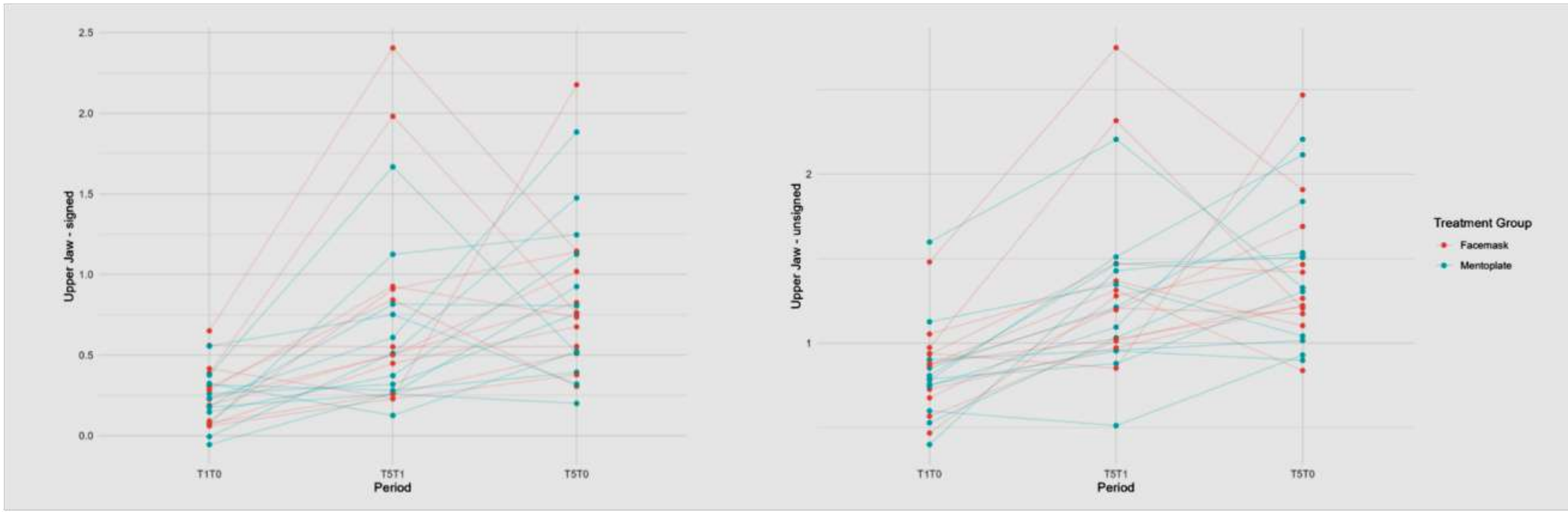


Figure 6.5: Scatter plot maxillary changes; T1T0: changes during active treatment (year 1); T5T1: changes during flow-up (year 1 – 5); T5T0: changes overall (start- year 5); Left: signed changes; right: unsigned changes.

Ancillary analyses

No ancillary analyses were done.

Harms

In our MP patient group, no plate loosening was observed. Although some issues with the anchor hooks (fracture or mucosal irritation) occurred, none led to treatment cessation. No mentoplate or screws required reinsertion. Fractures were managed by additional bending of the mentoplate, while mucosal irritation was resolved through optimized oral hygiene and the application of local chlorhexidine gel.

DISCUSSION

The primary aim of early intervention for Class III patients is to avoid orthognathic surgery when fully grown. This is done by promoting maxillary protrusion and restricting mandibular growth while mitigating unwanted outcomes like anterior shift of the upper dentition and vertical skeletal changes. Various strategies have been developed to achieve these objectives, such as facemask treatment or treatment with bone-anchors, which are used in conjunction with both intra- and extra-oral devices [10–24]. Treatment strategies with bone anchors have become increasingly more popular because they are often assumed to provide better skeletal control, and potential higher patient compliance [38–41]. Our findings suggest that this theoretical advantage may not translate to better long term skeletal treatment effect. Lack of prospective RCTs exist comparing the outcomes of different treatment protocols [5]. Only four prior RCTs have compared FM treatment to skeletal anchorage, and none of them report on long term results [4] . This scarcity of RCTs may stem from the challenges in convincing parents to enroll their children in a study where the treatment type is subject to randomization. To our knowledge, this study is the largest RCT with long term results comparing FM therapy with skeletal anchorage (MP) and the very first RCT to compare the long term effect of FM versus MP in combination with HH [4] . The assessment was conducted using a 3D approach which overcomes the limitations associated with lateral and frontal cephalograms, such as magnification error and distortion from structural superimposition.

Over five years, both FM and MP protocols produced similar skeletal treatment effects. These results align with Willmann et al.'s [42] short-term, retrospective 2D cephalometric study of 34 patients, which found comparable skeletal responses between HH with MP and FM. Our findings also support previous research showing that skeletal anchorage treatments do not produce significantly greater or faster skeletal changes than conventional methods [5,12,25]. However, direct comparisons with existing literature are limited, as most studies use 2D cephalometric analyses or linear and angular measurements based on cone beam CT scans rather than comprehensive 3D analysis.

Untreated Class III malocclusion tends to worsen with growth, characterized by excessive mandibular growth and a lack of maxillary catch-up growth [26,43]. This growth pattern persists beyond adolescence, with mandibular growth continuing until about 17 years in females and after 18 years in males [44]. Analysis of jaw growth patterns show that forward growth (signed values) accounts for approximately half of the total upper jaw growth (unsigned values), while in the lower jaw only 7% of total growth has a forward vector at the 5-year follow-up in the MP group and even a negative (backward) growth pattern in the FM group. While these results suggest elastic traction effectively guided growth direction, the lack of a control group limits definitive conclusions. Surprisingly, the growth patterns established in the first year continued through the later follow-up phase, even after discontinuing Class III elastic traction. The upper jaw maintained approximately 50% forward growth, while the lower jaw showed only 5-8% forward growth. This is also reflected in the differences observed in the GEE model, where similar signed mandibular changes between active treatment (T1-T0) and follow-up (T2-T1) were present. However, unsigned changes were significantly larger during follow-up ($p < 0.01$). This suggests that successful early treatment creates better functional conditions for natural growth resulting in a comparable growth pattern in succeeding years in the lower jaw. Males exhibited greater mandibular growth than females, with 0.17 mm more forward growth ($p=0.03$) and 0.28 mm more total growth ($p<0.01$). These findings align with previous studies showing enhanced mandibular growth in male Class III patients [45]. A large gonial angle, which indicates vertical growth pattern, correlated with mandibular growth in our patients for both signed ($p=0.05$) and unsigned ($p=0.01$)

changes. While some suggest that a large initial gonial angle may predict poor treatment outcomes, current evidence supporting this claim is limited [46,47]. Our findings demonstrate that increased gonial angles correlate with greater mandibular changes, though the impact on treatment outcomes remains uncertain.

A treatment protocol involving MP offers several potential advantages as a bone anchor compared to other options. It can be inserted in the lower jaw before the eruption of the mandibular canines, as it is fixed to the bone in the chin area below the mandibular incisors (Figure 6.1). This allows for earlier initiation of interceptive treatment. It has been suggested that early Class III treatment before the age 10 provides better results [30,48–53]. Additionally, the placement of the screws away from the tooth roots ensures the design safety, significantly reducing the risk of injuring adjacent teeth. In our study, no loosening of the MP was observed. This is likely due to its one-piece construction, which allows for simultaneous traction on both sides and a resultant force vector directed towards the mandibular bone, preventing plate loosening. In contrast, other bone anchor designs have a higher potential for loosening or interfering with the roots of adjacent teeth [27]. Some minor issues like plate fracture and mucosal irritation were observed in our study but did not lead to treatment cessation. Importantly, placing MP and palatal screws for the HH does not require an incision with periosteal stripping in the upper jaw, resulting in less swelling and postoperative discomfort compared to traditional bone anchors used in BAMP protocols. From a surgical perspective, MP is the anchor of choice due to its lower risk of loosening, fewer potential complications related to adjacent teeth, and reduced postoperative discomfort for the patient.

<u>Limitations</u>

The results were based on a 12-patient-per-group observation. Individual variation in growth patterns and genetic predisposition for class III malocclusion may significantly influence treatment outcomes, regardless of the intervention chosen. Our sample size, while statistically adequate, may not fully represent the spectrum of genetic variability in Class III patients. Significant patient dropout occurred at the five-year follow-up, also in the MP group. This was unexpected since MP patients typically return for hardware removal. Though all MP were eventually removed, the varying removal times extended beyond T2, leading to these patients' exclusion to avoid bias. Our study focused on comparing skeletal effects between the two protocols, rather than evaluating Class III malocclusion correction. While this approach may be less clinically intuitive, it provides objective quantification of skeletal changes. Our study analyzed complete 3D skeletal models. Future research should decompose the structures into distinct anatomical segments to provide a more detailed depiction of skeletal changes. This segmented approach would allow detailed analysis of dental, palatal, zygomatic, and soft tissue changes. Additionally, future studies should evaluate patient compliance and pain perception associated with MP. This RCT focused specifically on appliance design and mechanics and its findings challenge the common assumption that bone anchors provide superior results despite being more invasive.

Generalizability

Our results are primarily applicable to patients in the mixed dentition phase (average 9.7 ± 1.3 years) with moderate skeletal discrepancies. The findings may not extend to patients with severe skeletal class III malocclusions or those at different developmental stages.

As this trial was conducted in a single center with experienced clinicians, results might vary in different clinical settings. We used a standardized Alt-RAMEC protocol and force system. Different expansion protocols or force magnitudes might yield different outcomes.

Interpretation

It's challenging to distinguish between natural growth changes and treatment effects in Class III cases. Clinicians cannot reliably predict which patients will respond well to early intervention [46,47]. Patients and parents should be informed that 20-30% of cases may ultimately require orthognathic surgery, even after interceptive treatment [7,49,53–56]. The individual's growth pattern may be the most critical factor influencing outcomes, rather than the specific treatment technique employed. Early treatment success should be monitored closely during the first 6-12 months, as positive treatment effect potentially provides a better myofunctional situation for further growth. For those who do not respond well, it's often best to delay treatment until the patient has fully matured, at which point orthognathic surgery becomes the best option. Since both treatment protocols yield comparable skeletal effects in the long term, orthodontists may regard them as equally viable options for early class III treatment. This is particularly relevant for clinical decision making, as it suggests that the choice between FM and MP should be based on individual patient factors rather than presumed mechanical advantages. This consideration may encompass patient-specific factors such as compliance challenges or anatomical constraints.

Other information

Registration

This Randomized Clinical trial was registered at www.ClinicalTrials.gov (ID: NCT02711111) Ethical approval has been granted by the Ethics Committee at the Ziekenhuis Oost Limburg, Belgium (EudraCT B371201629565) (13/12/2016)

Conflicts of interest

The authors declare that they have no conflict of interest.

Data availability

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

Authors' contributions

Conceptualization, JM and RJ; methodology, JM and SS, software, SS formal analysis, JM and JT; investigation, JM; resources, JM and CP; data curation, JM; writing—original draft preparation, JM; writing—review and editing, JM, SS and RJ; visualization, JT; supervision, CP and RR; project administration, JM; All authors have read and agreed to the published version of the manuscript.

Funding

No funding was received.

REFERENCES

1. Hardy DK, Cubas YP, Orellana MF. Prevalence of angle class III malocclusion: A systematic review and meta-analysis. Open J Epidemiol [Internet]. 2012;02(04):75–82. Available from: http://www.scirp.org/journal/PaperInformation.aspx?PaperID=24715&#abstract
2. Woon SC, Thiruvenkatachari B. Early orthodontic treatment for Class III malocclusion: A systematic review and meta-analysis. Am J Orthod Dentofacial Orthop [Internet]. 2017 Jan;151(1):28–52. Available from: http://www.sciencedirect.com/science/article/pii/S0889540616305716
3. De Clerck H, Cevidanes L, Baccetti T. Dentofacial effects of bone-anchored maxillary protraction: A controlled study of consecutively treated Class III patients. American Journal of Orthodontics and Dentofacial Orthopedics. 2010;
4. Owens D, Watkinson S, Harrison JE, Turner S, Worthington H V. Orthodontic treatment for prominent lower front teeth (Class III malocclusion) in children (Review). Cochrane Database of Systematic Reviews. 2024;2024(4).
5. Cornelis MA, Tepedino M, Riis NDV, Niu X, Cattaneo PM. Treatment effect of bone-Anchored maxillary protraction in growing patients compared to controls: A systematic review with meta-Analysis. Eur J Orthod. 2021;43(1):51–68.
6. Wang J, Yang Y, Wang Y, Zhang L, Ji W, Hong Z, et al. Clinical effectiveness of different types of bone-anchored maxillary protraction devices for skeletal Class III malocclusion: Systematic review and network meta-analysis. Korean J Orthod. 2022;52(5):313–23.
7. Mandall N, Cousley R, Dibiase A, Dyer F, Littlewood S, Mattick R, et al. Early class III protraction facemask treatment reduces the need for orthognathic surgery: a multi-centre, two-arm parallel randomized, controlled trial. J Orthod. 2016;43(May 2017):164–75.
8. Mandall N, Aleid W, Cousley R, Curran E, Caldwell S, DiBiase A, et al. The effectiveness of bone anchored maxillary protraction (BAMP) in the management of class III skeletal malocclusion in children aged 11–14 years compared with an untreated control group: A multicentre two-arm parallel randomised controlled trial. J Orthod. 2024;
9. Ngan PW, Hagg U, Yiu C, Wei SH. Treatment response and long-term dentofacial adaptations to maxillary expansion and protraction. Semin Orthod. 1997;3(4):255–64.
10. de Clerck HJ, Proffit WR. Growth modification of the face: A current perspective with emphasis on Class III treatment. American Journal of Orthodontics and Dentofacial Orthopedics. 2015;148(1):37–46.
11. Cevidanes L, Baccetti T, Franchi L, McNamara JA, De Clerck H. Comparison of two protocols for maxillary protraction: bone anchors versus face mask with rapid maxillary expansion. Angle Orthod [Internet]. 2010 Sep [cited 2017 Jul 17];80(5):799–806. Available from: http://www.angle.org/doi/10.2319/111709-651.1
12. Rodríguez de Guzmán-Barrera J, Sáez Martínez C, Boronat-Catalá M, Montiel-Company JM, Paredes-Gallardo V, Gandía-Franco JL, et al. Effectiveness of interceptive treatment of class III malocclusions with skeletal anchorage: A systematic review and meta-analysis. Bencharit S, editor. PLoS One [Internet]. 2017 Mar 22 [cited 2017 Apr 5];12(3):e0173875. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5362089/pdf/pone.0173875.pdf
13. Nienkemper M, Wilmes B, Franchi L, Drescher D. Effectiveness of maxillary protraction using a hybrid hyrax-facemask combination: *A controlled clinical study*. Angle Orthod [Internet]. 2015 Sep [cited 2017 Apr 5];85(5):764–70. Available from:

http://www.ncbi.nlm.nih.gov/pubmed/25393800
14. Wilmes B, Ludwig B, Katyal V, Nienkemper M, Rein A, Drescher D. The Hybrid Hyrax Distalizer, a new all-in-one appliance for rapid palatal expansion, early class III treatment and upper molar distalization. J Orthod [Internet]. 2014 Sep 16 [cited 2017 Apr 5];41(sup1):s47–53. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25138366
15. Bozkaya E, Yüksel AS, Bozkaya S. Zygomatic miniplates for skeletal anchorage in orthopedic correction of Class III malocclusion: A controlled clinical trial. The Korean Journal of Orthodontics [Internet]. 2017 Mar [cited 2017 Apr 5];47(2):118. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28337421
16. Şar Ç, Şahinoğlu Z, Özçirpici AA, Uçkan S. Dentofacial effects of skeletal anchored treatment modalities for the correction of maxillary retrognathia. American Journal of Orthodontics and Dentofacial Orthopedics. 2014;145(1).
17. Enacar A, Giray B, Pehlivanoglu M, Iplikcioglu H. Facemask therapy with rigid anchorage in a patient with maxillary hypoplasia and severe oligodontia. Am J Orthod Dentofacial Orthop [Internet]. 2003 May [cited 2017 Jul 17];123(5):571–7. Available from: http://www.mosby.com/scripts/om.dll/serve?action=searchDB&searchDBfor=art&artType=abs&id=amod03571
18. Hong H, Ngan P, Han GL, Liu GQ, Wei SHY. Use of onplants as stable anchorage for facemask treatment: A case report. Angle Orthodontist. 2005;75(3):453–60.
19. Jamilian A, Showkatbakhsh R. Treatment of maxillary deficiency by miniscrew implants--a case report. J Orthod [Internet]. 2010 Mar 16 [cited 2017 Jul 17];37(1):56–61. Available from: http://www.tandfonline.com/doi/full/10.1179/14653121042876
20. Kaya D, Kocadereli I, Kan B, Tasar F. Effects of facemask treatment anchored with miniplates after alternate rapid maxillary expansions and constrictions; a pilot study. Angle Orthod [Internet]. 2011 Jul [cited 2017 Jul 17];81(4):639–46. Available from: http://www.angle.org/doi/10.2319/081010-473.1
21. Kircelli BH, Pektaş ZO, Uçkan S. Orthopedic protraction with skeletal anchorage in a patient with maxillary hypoplasia and hypodontia. Angle Orthodontist [Internet]. 2006 Jan [cited 2017 Jul 17];76(1):156–63. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16448286
22. Lee NK, Yang IH, Baek SH. The short-term treatment effects of face mask therapy in Class III patients based on the anchorage device: miniplates vs rapid maxillary expansion. Angle Orthod [Internet]. 2012 Sep [cited 2017 Jul 17];82(5):846–52. Available from: http://www.angle.org/doi/10.2319/090811-584.1
23. Baek SH, Kim KW, Choi JY. New treatment modality for maxillary hypoplasia in cleft patients. Protraction facemask with miniplate anchorage. Angle Orthod [Internet]. 2010 Jul [cited 2017 Jul 17];80(4):783–91. Available from: http://www.angle.org/doi/10.2319/073009-435.1
24. Sar C, Arman-Özçırpıcı A, Uçkan S, Yazıcı AC. Comparative evaluation of maxillary protraction with or without skeletal anchorage. Am J Orthod Dentofacial Orthop [Internet]. 2011 May [cited 2017 Jul 17];139(5):636–49. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0889540611001314
25. Meyns J, Brasil DM, Mazzi-Chaves JF, Politis C, Jacobs R. The clinical outcome of skeletal anchorage in interceptive treatment (in growing patients) for class III malocclusion. Int J Oral Maxillofac Surg [Internet]. 2018;47(8):1003–10. Available from: https://doi.org/10.1016/j.ijom.2018.04.011
26. Rutili V, Nieri M, Franceschi D, Pierleoni F, Giuntini V, Franchi L. Effects produced by the facemask with and without skeletal anchorage for the orthopaedic treatment of Class III malocclusion in growing patients: a systematic review and meta-analysis of RCTs. Eur J Orthod. 2022;1–12.

27. Van Hevele J, Nout E, Claeys T, Meyns J, Scheerlinck J, Politis C. Bone-anchored maxillary protraction to correct a class III skeletal relationship: A multicenter retrospective analysis of 218 patients. Journal of Cranio-Maxillofacial Surgery [Internet]. 2018;46(10):1800–6. Available from: https://doi.org/10.1016/j.jcms.2018.07.007
28. Bozkaya E, Yüksel AS, Bozkaya S. Zygomatic miniplates for skeletal anchorage in orthopedic correction of Class III malocclusion: A controlled clinical trial. The Korean Journal of Orthodontics [Internet]. 2017 Mar [cited 2017 Apr 5];47(2):118. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28337421
29. Wilmes B, Nienkemper M, Drescher D. Application and effectiveness of a mini-implant- and tooth-borne rapid palatal expansion device: the hybrid hyrax. World J Orthod [Internet]. 2010 [cited 2017 Jul 17];11(4):323–30. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21490997
30. Kim JH, Viana M a, Graber TM, Omerza FF, BeGole E a. The effectiveness of protraction face mask therapy: a meta-analysis. Am J Orthod Dentofacial Orthop. 1999;115(6):675–85.
31. Foersch M, Jacobs C, Wriedt S, Hechtner M, Wehrbein H. Effectiveness of maxillary protraction using facemask with or without maxillary expansion: a systematic review and meta-analysis. Clin Oral Investig. 2015;19(6):1181–92.
32. Pithon MM, De N, Santos L, Barreto CR, Santos D, Carvalho F, et al. Is alternate rapid maxillary expansion and constriction an effective protocol in the treatment of Class III malocclusion? A systematic review Is alternate rapid maxillary expansion and constriction protocol effective in the treatment of Class III maloc- c. Dental Press J Orthod Dental Press J Orthod Dental Press J Orthod [Internet]. 2016 [cited 2017 Apr 24];212121(666):34–4234. Available from: http://dx.doi.org/10.1590/2177-6709.21.6.034-042.oar
33. Liou EJW, Tsai WC. A new protocol for maxillary protraction in cleft patients: Repetitive weekly protocol of alternate rapid maxillary expansions and constrictions. Cleft Palate-Craniofacial Journal. 2005;42(2):121–7.
34. Maes F, Collignon A, Vandermeulen D, Marchal G, Suetens P. Multi-modality image registration by maximization of mutual information. Proceedings of the Workship on Mathematical Methods in Biomedical Image Analysis. 1996;16(2):14–22.
35. Pluim JPW, Maintz JBAA, Viergever MA. Mutual-information-based registration of medical images: A survey. IEEE Trans Med Imaging. 2003;22(8):986–1004.
36. Nguyen T, Cevidanes L, Franchi L, Ruellas A, Jackson T. Three-dimensional mandibular regional superimposition in growing patients. American Journal of Orthodontics and Dentofacial Orthopedics [Internet]. 2018;153(5):747–54. Available from: https://doi.org/10.1016/j.ajodo.2017.07.026
37. Cericato GO, Bittencourt MA V, Paranhos LR. Validity of the assessment method of skeletal maturation by cervical vertebrae: a systematic review and meta-analysis.
38. De Clerck HJ, Proffit WR. Growth modification of the face: A current perspective with emphasis on Class III treatment. American Journal of Orthodontics and Dentofacial Orthopedics. 2015.
39. Tarraf NE, Dalci O, Dalci K, Altug AT, Darendeliler MA. A retrospective comparison of two protocols for correction of skeletal Class III malocclusion in prepubertal children: hybrid hyrax expander with mandibular miniplates and rapid maxillary expansion with face mask. Prog Orthod. 2023;24(1).
40. Elnagar MH, Elshourbagy E, Ghobashy S, Khedr M, Evans CA. Comparative evaluation of 2 skeletally anchored maxillary protraction protocols. Am J Orthod Dentofacial Orthop [Internet]. 2016 Nov [cited 2017 Jul 17];150(5):751–62. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0889540616303948
41. Hino CT, Cevidanes LHS, Nguyen TT, De Clerck HJ, Franchi L, McNamara

JA. Three-dimensional analysis of maxillary changes associated with facemask and rapid maxillary expansion compared with bone anchored maxillary protraction. American Journal of Orthodontics and Dentofacial Orthopedics. 2013;
42. Willmann JH, Nienkemper M, Tarraf NE, Wilmes B, Drescher D. Early Class III treatment with Hybrid-Hyrax – Facemask in comparison to Hybrid-Hyrax-Mentoplate – skeletal and dental outcomes. Prog Orthod. 2018;19(1):0–7.
43. Baccetti T, Franchi L, McNamara Jr JA. Growth in the Untreated Class III Subject. Semin Orthod [Internet]. 2007 Sep 1;13(3):130–42. Available from: https://doi.org/10.1053/j.sodo.2007.05.006
44. Rutili V, Nieri M, Giuntini V, McNamara JA, Franchi L. A multilevel analysis of craniofacial growth in subjects with untreated Class III malocclusion. Orthod Craniofac Res. 2020;23(2):181–91.
45. Baccetti T, Reyes BC, McNamara JA. Craniofacial changes in Class III malocclusion as related to skeletal and dental maturation. American Journal of Orthodontics and Dentofacial Orthopedics. 2007;132(2):171.e1-171.e12.
46. Choi YJ, Chang JE, Chung CJ, Tahk JH, Kim KH. Prediction of long-term success of orthopedic treatment in skeletal Class III malocclusions. American Journal of Orthodontics and Dentofacial Orthopedics [Internet]. 2017;152(2):193–203. Available from: http://dx.doi.org/10.1016/j.ajodo.2016.12.018
47. Fudalej P, Dragan M, Wedrychowska-Szulc B. Prediction of the outcome of orthodontic treatment of Class III malocclusions-a systematic review. Eur J Orthod. 2011;33(2):190–7.
48. Baccetti T, McGill JS, Franchi L, McNamara JAJ, Tollaro I. Skeletal effects of early treatment of Class III malocclusion with maxillary expansion and face-mask therapy. Am J Orthod Dentofacial Orthop. 1998 Mar;113(3):333–43.
49. Baccetti T, Franchi L, McNamara JA. Treatment and posttreatment craniofacial changes after rapid maxillary expansion and facemask therapy. American Journal of Orthodontics and Dentofacial Orthopedics. 2000;118(4):404–13.
50. Kapust AJ, Sinclair PM, Turley PK. Cephalometric effects of face mask/expansion therapy in Class III children: a comparison of three age groups. Am J Orthod Dentofacial Orthop. 1998 Feb;113(2):204–12.
51. Franchi L, Baccetti T, McNamara JA. Postpubertal assessment of treatment timing for maxillary expansion and protraction therapy followed by fixed appliances. Am J Orthod Dentofacial Orthop. 2004 Nov;126(5):555–68.
52. Kajiyama K, Murakami T, Suzuki A. Comparison of orthodontic and orthopedic effects of a modified maxillary protractor between deciduous and early mixed dentitions. American Journal of Orthodontics and Dentofacial Orthopedics. 2004;126(1):23–32.
53. Wells AP, Sarver DM, Proffit WR. Long-term efficacy of reverse pull headgear therapy. Angle Orthodontist. 2006;76(6):915–22.
54. Hagg U, Tse A, Bendeus M, Rabie ABM. Long-term follow-up of early treatment with reverse headgear. Eur J Orthod. 2003;25:95–102.
55. Masucci C, Franchi L, Defraia E, Mucedero M, Cozza P, Baccetti T. Stability of rapid maxillary expansion and facemask therapy: A long-term controlled study. American Journal of Orthodontics and Dentofacial Orthopedics. 2011;140(4):493–500.
56. Gebeile-Chauty S, Perret M, Schott AM, Aknin JJ. [Early treatment of Class III: a long-term cohort study]. Orthod Fr. 2010 Sep;81(3):245–54.

SUPPLEMENTARY MATERIAL

Supplementary material 1: Details randomization sequence

Supplementary material 2: Volumetric changes per patient

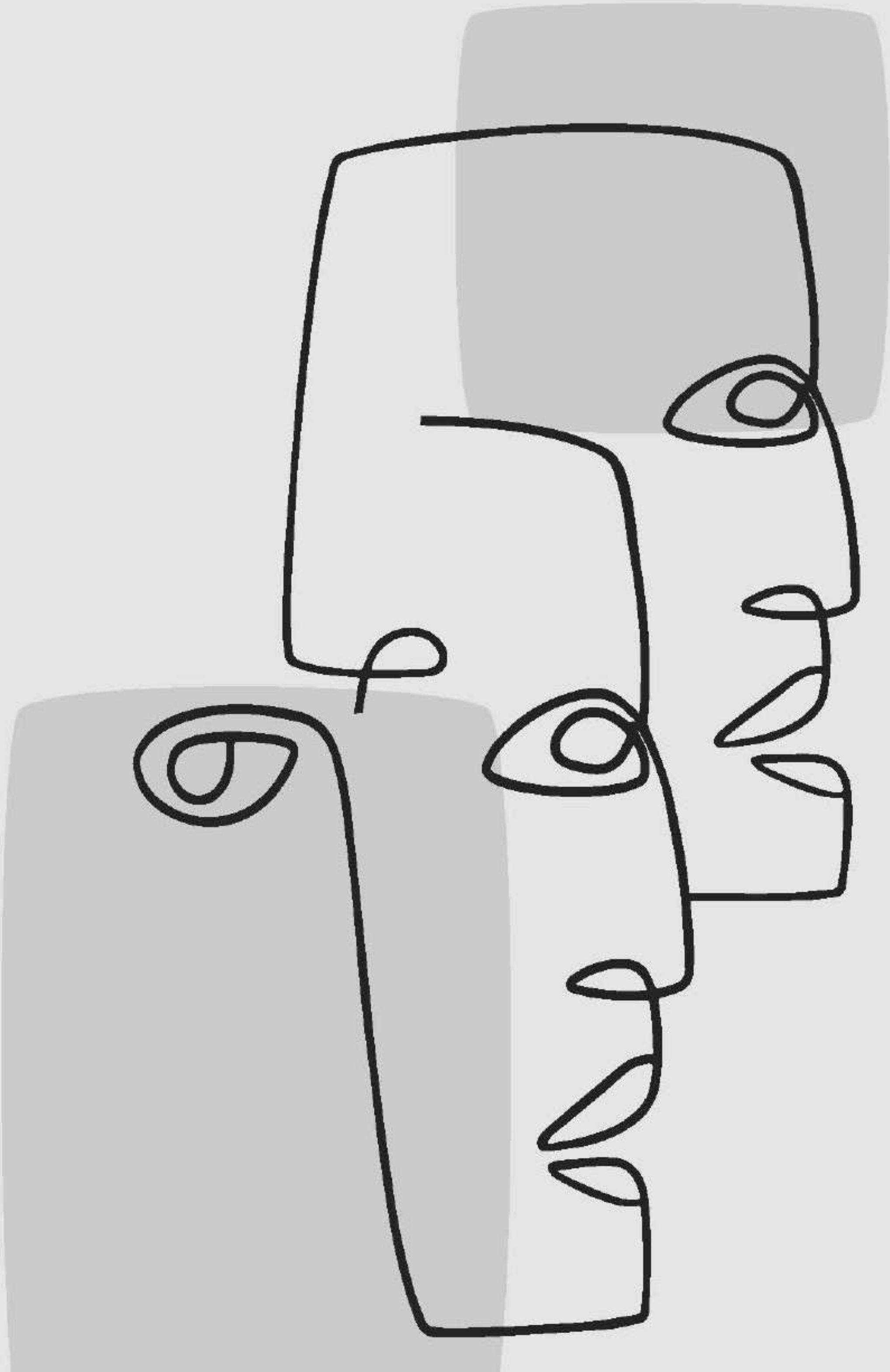
S1: details randomization sequence

nr	date of enrollment	T0 baseline-scan	T1 one-year scan	T2 five-year scan	F / M	type of treatment	T0-T1 (months)	T0-T2 (months)
1	16/12/2016	14/02/2017	10/04/2018	8/02/2023	M	MP	13	71
2	16/12/2016	2/05/2017	27/02/2018	21/10/2022	F	MP	9	65
3	19/12/2016	28/02/2017	27/02/2018	21/10/2022	F	FM	11	67
4	21/12/2016	14/02/2017	21/02/2018	/	F	MP	12	/
5	21/12/2016	21/03/2017	21/02/2018	21/10/2022	M	MP	11	67
6	17/01/2017	21/03/2017	2/03/2018	21/10/2022	M	MP	11	67
7	24/01/2017	24/02/2017	21/02/2018	26/10/2022	M	FM	11	68
8	7/03/2017	4/04/2017	2/03/2018	15/03/2023	F	FM	10	71
9	15/03/2017	27/06/2017	22/06/2018	8/02/2023	F	MP	11	67
10	21/03/2017	6/10/2017	26/03/2019	9/11/2022	F	FM	17	61
11	28/03/2017	20/06/2017	22/06/2018	26/10/2022	F	MP	12	64
12	31/03/2017	5/05/2017	3/07/2018	9/11/2022	M	FM	13	66
13	31/03/2017	5/05/2017	3/07/2018	9/11/2022	F	FM	13	66
14	9/05/2017	14/11/2017	30/11/2018	8/02/2023	F	MP	12	62
15	9/08/2017	12/09/2017	17/07/2018	26/10/2022	M	MP	10	61
16	22/09/2017	27/11/2017	22/01/2019	1/02/2024	F	MP	13	74
17	26/09/2017	4/12/2017	/	/	F	MP	/	/
18	2/10/2017	18/10/2017	15/01/2019	15/03/2023	M	MP	14	64
19	17/10/2017	28/11/2017	22/01/2019	4/09/2023	M	FM	13	69
20	18/10/2017	21/11/2017	22/01/2019	9/11/2022	F	FM	14	59
21	24/10/2017	27/11/2017	15/01/2019	15/03/2023	M	MP	13	63
22	9/01/2018	27/02/2018	12/03/2019	/	M	FM	12	/
23	30/01/2018	2/03/2018	13/03/2019	/	M	FM	12	/
24	2/03/2018	2/03/2018	29/01/2019	4/09/2023	M	FM	10	66
25	1/06/2018	12/06/2018	14/05/2019	8/02/2023	F	MP	11	55
26	8/06/2018	8/06/2018	11/06/2019	30/08/2023	F	FM	12	62
27	27/06/2018	27/06/2018	25/06/2019	20/12/2023	M	FM	11	65
28	7/09/2018	19/09/2018	7/08/2019	26/10/2022	M	FM	10	49
						Mean	12,00	64,54
						SD	1,59	5,21

S2: Volumetric changes per patient

	T0 - T1				T1 - T2				T0 - T2			
	Maxilla		Mandible		Maxilla		Mandible		Maxilla		Mandible	
	S mean	US mean	S mean	US mean	S mean	US mean	S mean	US mean	S mean	US mean	S mean	US mean
MP1	0,3153	0,9014	0,0715	0,3501	0,2812	0,9575	0,1516	1,4410	0,3927	1,0152	-0,1333	1,0230
MP2	0,0697	0,3981	0,081	0,8046	1,1249	1,4274	0,1544	1,7943	1,2459	1,5342	0,0269	1,6464
MP3	0,2599	0,7874	0,191	0,5275	0,3186	0,8782	-0,0476	0,7742	0,7566	1,3044	0,221	1,0226
MP4	0,1771	0,7549	0,1231	0,5483	0,259	0,9532	0,0292	0,6264	0,2001	0,8976	0,207	0,8766
MP5	0,147	0,8514	-0,0265	0,5317	0,3726	1,2119	-0,1565	1,4304	1,1255	1,8376	-0,3237	1,4948
MP6	0,5553	1,126	0,1291	0,496	0,7513	1,3465	-0,1256	0,7243	0,3201	1,0417	0,0912	1,1802
MP7	-0,0554	0,5279	0,0879	0,4142	0,262	1,0308	0,7634	1,7281	0,9247	1,5166	0,9957	2,0475
MP8	-0,0058	0,781	-0,0222	0,5031	0,51	1,5099	-0,0107	1,3536	1,4743	2,1141	-0,1878	1,3341
MP9	0,1807	0,8062	0,1395	0,8181	0,8159	1,4669	-0,4221	1,2168	0,8059	1,5065	-0,1234	1,5805
MP10	0,2316	0,7449	0,1036	0,8201	0,609	1,0942	0,3548	1,0586	1,8831	2,2054	0,1751	1,1066
MP11	0,3758	1,5976	-0,1168	0,4496	1,6674	2,205	0,5164	1,7741	0,5157	1,3275	0,1021	1,4633
MP12	0,3235	0,5982	0,0379	0,4487	0,1255	0,5112	0,0014	0,5983	0,5233	0,9285	0,1647	0,8108
FM1	0,3025	0,8712	0,6637	1,4764	0,8424	1,3127	-0,1512	0,7723	0,3069	0,837	-0,0088	0,9696
FM2	0,5589	1,0534	-0,0406	0,4086	0,5509	1,3672	-0,1192	0,5642	0,5536	1,1029	-0,074	0,8186
FM3	0,0671	0,6751	-0,0178	0,5944	0,4483	1,2065	0,4441	1,4523	0,6751	1,1734	0,1258	1,2847
FM4	0,6501	1,4796	0,0406	0,5554	2,4044	2,7473	-0,0258	1,0944	1,1438	1,9073	-0,2576	0,8931
FM5	0,188	0,5661	-0,2119	0,5166	0,5051	1,012	-0,297	0,9645	0,825	1,2639	-0,4793	1,24
FM6	0,0792	0,7259	-0,0525	0,4993	0,2586	0,9721	0,043	1,3919	0,5103	1,2224	-0,0381	1,5446
FM7	0,0602	0,8798	-0,0149	0,6894	0,2285	1,0247	-0,0453	0,9252	0,3775	1,2159	-0,0212	1,2165
FM8	0,4157	0,9385	-0,0706	0,4594	0,2315	0,851	-0,1774	1,102	2,1764	2,4671	-0,1735	1,2237
FM9	0,386	0,9734	0,0762	0,5622	1,9805	2,3159	0,6483	1,6561	0,7633	1,206	0,4514	1,5518
FM10	0,2829	0,9329	0,0104	0,8735	0,9256	1,4711	0,2494	1,2144	0,736	1,4191	0,0125	1,2567
FM11	0,2282	0,8684	-0,0336	0,5916	0,5009	1,1963	0,0885	1,3049	1,0182	1,6897	0,1023	1,3457
FM12	0,0912	0,4671	0,0241	0,4246	0,9087	1,2787	0,2052	0,8726	1,1403	1,464	0,2857	0,939

T0: baseline; T1: 1 year; T2: 5 years
S: signed changes
US: unsigned changes



SECTION 4: Treatment outcome prediction

CHAPTER 7

Two-Dimensional analysis for predicting class III malocclusion treatment outcome.

This chapter is based on the following manuscript.

Meyns J., Van Caesbroeck K., Jazil O., Jindanil T., Shujaat S., Politis C., Jacobs R. Comparing long-term outcomes of facemask versus mentoplate therapy in skeletal class III malocclusion: a 5-year Randomized Controlled Trial. *Under review with Plos One*

ABSTRACT

Background:

Early intervention in skeletal class III malocclusion may reduce the need for orthognathic surgery, but evidence comparing traditional and bone-anchored approaches remains limited.

Objective:

To compare the efficacy of face mask (FM) versus bone-anchored mentoplate (MP) therapy combined with Alt-RAMEC in preventing orthognathic surgery for class III malocclusion.

Methods:

In this single-center, parallel-group randomized controlled trial, 28 skeletal class III patients (14 females, 14 males; mean age 9.7±1.3 years) were randomly assigned (1:1 allocation) to receive either Hybrid Hyrax + Facemask (FM group) or Hybrid Hyrax + Mentoplate (MP group). Treatment effect was assessed at baseline, one year, and five years using virtual lateral cephalograms generated from low-dose CT scans. Outcomes include the need for orthognathic surgery at five years (primary outcome), determined by blind assessment from 18 evaluators (orthodontists, surgeons, and laypersons) who reviewed standardized virtual patient models. Secondary outcome was cephalometric analysis of the treatment effect and identification of potential predictive cephalometric factors.

Results:

Twenty-two patients completed the five-year follow-up (mean age 15.5 years). The FM group showed a higher success rate in preventing orthognathic surgery need compared to the MP group (81% vs. 69%), though this difference was not statistically significant (p=0.43). Cephalometric analysis revealed similar outcomes between groups, except for SNO measurements, which were significantly higher in the FM group at five years (p=0.02). None of the investigated predictive cephalometric parameter correlated with treatment outcome.

Harms: minor harms were encountered with the anchor hooks (fracture or mucosal irritation), however none led to treatment cessation

Conclusions:

Both FM and MP protocols effectively reduced orthognathic surgery need, with no significant difference between approaches. However, approximately 26% of treated patients may still require surgery. Patient characteristics may be more influential than treatment method choice.

INTRODUCTION

Rationale

Treating patients with skeletal Class III malocclusions is one of the most challenging orthodontic problems. Treatment options vary by age: young patients may receive growth modification therapy, while adolescents and adults may undergo either orthodontic camouflage or orthognathic surgery after growth is complete. A common growth modification option is face mask (FM) therapy, alone or with rapid palatal expansion (RPE)[1] . The effectiveness of different orthopedic treatment techniques can vary depending on how the forces are applied to the jaw. Techniques that transfer forces through the teeth tend to have less impact on the underlying skeletal structure. To overcome the limitations of conventional FM therapy and to address more severe class III deformities, various skeletal anchorage techniques have gained popularity and are used in conjunction with both intraoral and extraoral appliances [2–12] . Studies suggest that symphyseal plates (such as Mentoplates) provide better vertical control in high-angle patients [13–15], although this improvement is likely to be due to the type of anchorage device used in the maxilla [16]. Despite the widespread use of skeletal anchorage for Class III interceptive treatment, there is currently no consensus on indications, techniques, age, protocols or forces used [17,18]. In addition, there is still no evidence that skeletal anchorage provides more or better outcomes [4,17,19], and the long-term stability of the treatment effect provided by bone anchors remains to be investigated [17–20].

It is difficult for clinicians to predict the extent and timing of skeletal growth. In addition, the eligibility of patients for early class III treatment remains controversial [21–24]. Clinicians are sometimes faced with questionable or poor results in terms of occlusion or facial aesthetics, even when the initial treatment effect appears good [24] . Over time, as the patient matures, relapse may occur, resulting in a less than ideal final outcome. There is limited research on the long-term outcomes of early treatment of Class III malocclusions with skeletal anchorage [18,20,25]. It is important to identify patients who are likely to benefit from interceptive treatment with minimal risk of relapse. For those unlikely to respond well, delaying treatment until growth is complete, followed by orthognathic surgery, may be a more effective strategy. Predictors of treatment success are often derived from 2D cephalometric analyses or linear/angular measurements from cone beam computed tomography (CBCT) scans [26–28]. Emerging models now integrate these measures with initial treatment response to optimize decision making and reduce the likelihood of unsuccessful outcomes [29]. However, most of this research is retrospective and lacks adequate validation in new cases, making their predictive accuracy uncertain [26]. The main goal of interceptive Class III treatment is to prevent orthognathic surgery. While previous studies have shown that both FM and Bone-anchored approaches may reduce the need for surgery by approximately 30 %, long term comparative data between both treatment approaches is lacking [13,20,21]. Determining the need for orthognathic surgery lacks standardized criteria or objective measurements [30,31]. While the Index of Orthognathic Functional Treatment Need (IOFTN) provides a reliable assessment of functional needs [32], it may not consider all relevant factors [33,34].

Objective

Therefore, the overall aim of the present 5-year follow-up randomized clinical trial was to compare the effectiveness of FM and MP treatments in preventing orthognathic surgery. To overcome the shortcomings of the IOFTN, a diverse panel consisting of orthodontists, oral and maxillofacial surgeons, and laypeople evaluated each patient and made binary decisions (yes/no) regarding treatment needs, including orthognathic surgery. A secondary aim of the present study was to assess whether the pretreatment 2D cephalometric measures could predict treatment success.

MATERIAL AND METHODS

Study design

This single center 2-arm parallel randomized controlled trial with a 1:1 allocation ratio, employed a two-phase evaluation approach: quantitative assessment of treatment outcomes through cephalometric analysis and qualitative evaluation of treatment necessity through a blinded panel survey.

Trial registration and ethical approval

This Randomized Clinical trial was registered at www.ClinicalTrials.gov (ID: NCT02711111). Ethical approval has been granted by the Ethics Committee at the Ziekenhuis Oost Limburg, Belgium (EudraCT B371201629565) (13/12/2016). Ethical approval for the inclusion of the control group in the survey analysis was obtained from the Clinical Trial Center (CTC) at KU Leuven, Belgium (ID: S67723) and the Ethics Committee Research UZ/KU Leuven (EudraCT/B-nr B371201629565).

Participants

28 patients were allocated to either treatment-protocols using sequentially numbered opaque, sealed envelopes. The randomization sequence was generated with a 1:1 allocation ratio. Patient recruitment occurred from 16 December 2016 to 7 September 2018. Scans were performed in three phases: initial scans (T0) from February 2017 to September 2018, first follow-up (T1) from February 2018 to August 2019, and second follow-up (T2) from October 2022 to February 2024. One patient was lost at the one-year follow-up and an additional five patients were lost at the 5-year follow-up: FM group (11 patients, 6 female and 5 male) and MP group (11 patients, 5 female and 6 male) (Figure 7.1, table 7.1). All patients had a skeletal Class III malocclusion in the mixed dentition characterized by an anterior crossbite or incisor end-to-end relationship, and Class III molar relationship. Exclusion criteria were: Cleft or craniofacial syndrome, previous orthodontic treatment, previous surgical intervention, significant skeletal asymmetry and functional class III malocclusion. The placement of the screws and MP was performed by the same surgeon. Orthodontic treatment was carried out by three orthodontists in private practice, all treating FM and MP patients. The initial severity of Class III malocclusion did not show a statistically significant difference between the two groups and both groups were age and gender matched (table 7.1, table 7.2).

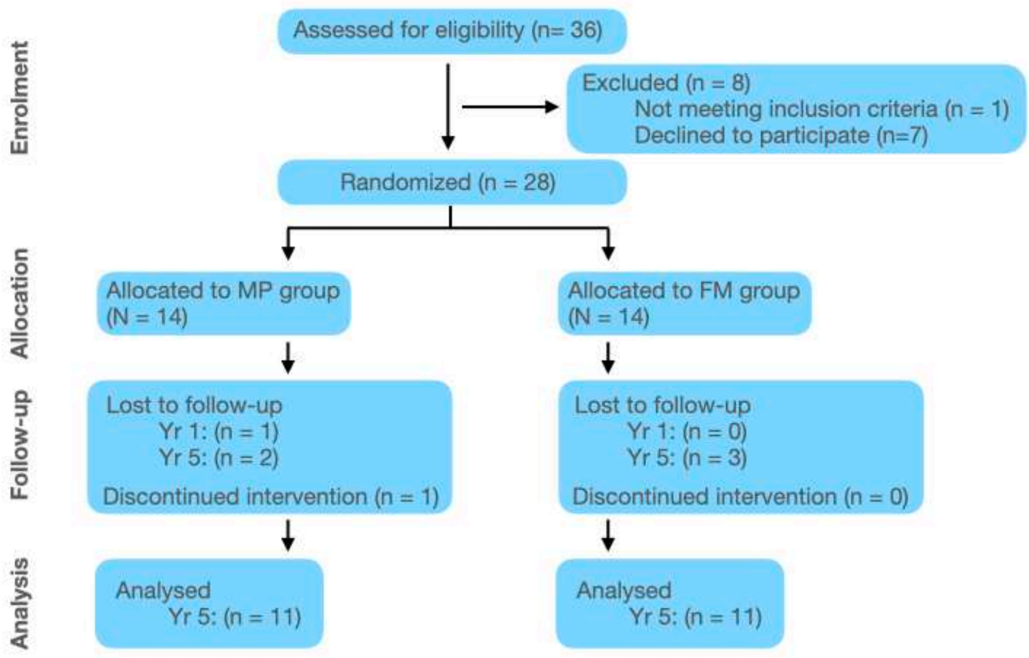


Figure 7.1: Flow diagram of patients' allocations in the trial

<u>Interventions</u>

Expansion (Alt-RAMEC)

In all study group patients, 2 selfdrilling mini-screws (Benefit miniscrews, PSM-medical solutions®, Gunningen, Germany) (2 mm in diameter and 9 mm long) were placed in the anterior palate, around the third rugae. A Hybrid Hyrax device (HH) was constructed with an expansion screw (Forestadent®, Sjeboygan, USA) and welded to bands. These bands were cemented with a light cured cement (Band-Lok®, Reliance Orthodontic Products, Thorndale, USA) to the first upper molars (figure 7.2). We used the Alt-RAMEC protocol where the hyrax was activated by the patient's parents twice a day (0.25 mm per turn, two turns in the morning and two turns at night) for 1 week, then it was deactivated twice a day (two turns in the morning and two turns at night) for 1 week [35]. This alternating protocol was repeated three times. In the next week the maxilla was set in the correct transverse dimension.

Face mask group (FM)

The patients were given FM (Orthocomfort & Medical Distributors SL®, Barcelona, Spain) and Alt-RAMEC simultaneously (figure 7.2). Elastics were attached from the hooks of the expander to the facemask in a downward and forward vector, producing orthopedic forces of 360 - 400 g per side (equivalent to 12,7 – 14 oz). The FM group was instructed to use it for 12–14 h a day overnight during the first 6 months or until a positive overjet of ≧ 2 mm was reached. The next 6 months the FM was only worn during sleep.

Mentoplate group (MP)

A MP (PSM-medical solutions®, Gunningen, Germany) was placed during general anesthesia trough a marginal gingival incision. The plate was bent and modified before fixation with 2 to 4 screws (KLS Martin®, Tuttlingen, Germany). The patients were given Alt-RAMEC and protraction elastics simultaneously, producing orthopedic forces of 185 g per side (6 ½ oz) (figure 7.2). The MP group was instructed to use it for 24 h a day, 7d a week, including meals, and to replace the elastics once a day during the first 6 months or until a positive overjet of ≧ 2 mm was reached. The next 6 months the elastics were only worn during sleep.

Fixed appliances

After phase 1 treatment (interceptive maxillary protraction) all patients received identical full fixed orthodontic appliances (edgewise mechanics, MBT .022 slot, Empower R, American Orthodontics®)) during phase 2. Also no elastic traction was employed during phase 2, after the one year (T1) time-point. The treating orthodontists followed standardized techniques for both treatment phases (supporting file 1 for details regarding the orthodontic protocol). In three MP patients and one FM patient, four premolar extractions were required. Additionally, one FM patient underwent the extraction of two premolars in the lower jaw.

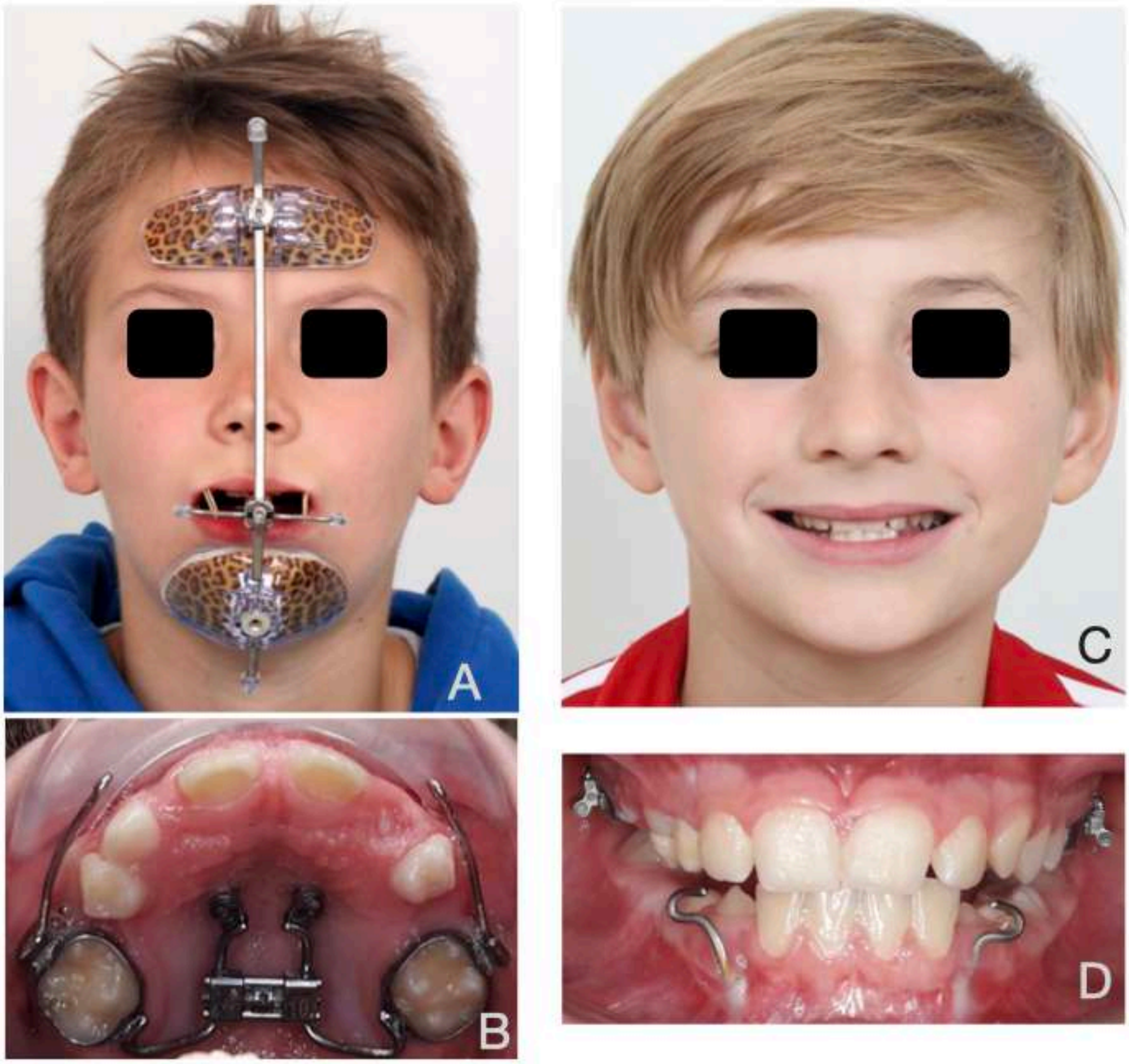


Figure 7.2: Facemask-treatment: A. extra-oral view, B. intra-oral view; Mentoplate-treatment: C extra-oral view, D. intra-oral view; Hybrid-Hyrax (B)

Table 7.1: Number, Age and duration of treatment

	N (Female/Male)			Age (mean)			Duration of treatment (mean in months)	
Group	T0	T1	T2	T0	T1	T2	T0-T1	T0-T2
FM	14 (7 / 7)	14 (7/ 7)	11 (6/ 5)	9 y, 6 mo	10 y, 0 mo	15 y, 5 mo	12 mo	64 mo
MP	14 (7 / 7)	13 (6 /7)	11 (5 /6)	9 y, 7 mo	10 y, 7 mo	15 y, 4 mo	11,7 mo	65 mo

FM: Facemask; MP: Mentoplate; T0: baseline; T1: 1 year follow-up; T2: 5-year follow-up

Table 7.2: cephalometric values at T0 and T2.

	Group characteristics at T0			Group characteristics at end of treatment (T2)			Changes T2-T0		
	Facemask Mean ± SD	**Mentoplate** Mean ± SD	p-value	**Facemask** Mean ± SD	**Mentoplate** Mean ± SD	p-value	**Facemask** Mean ± SD	**Mentoplate** Mean ± SD	p-value
Sagittal									
SNA °	79.08 ± 2.29	77.93 ± 3.64	0,38	81.67 ± 2.58	80.44 ± 5.31	0.50**	2.59 ± 2.98	2.51 ± 2.29	0,94
SNB °	79.78 ± 2.07	78.64 ± 4.58	0,46**	80,82 ± 3.19	79.49 ± 5.14	0,48	1.04 ± 2.67	0.85 ± 1.59	0,85
ANB °	-0.72 ± 2.17	-0.70 ± 1.52	0.57 *	0.86 ± 3.05	0.94 ± 1.41	0.94**	1.58 ± 3.48	1.64 ± 2.00	0,96
Wits (mm)	-6.0 ± 1.73	-5.64 ± 2.58	0,35	-3.09 ± 2.21	-4.27 ± 2.72	0,28	2.91 ± 2.84	1.36 ± 2.98	0,23
SNO	54.73 ± 3.91	52.82 ± 3.12	0,19	57.45 ± 2.54	53.36 ± 4.50	0.02	2.73 ± 1.21	0.55 ± 3.78	0.09**

Mean ± SD: standard deviation; p-value: Unpaired two-sided samples t-test; *p-value: Wilcoxon two sided test; ** p-value: Welch's two-sided t-test

Outcome assessment

Our study employed two complementary approaches to evaluate treatment outcomes: objective cephalometric analysis and subjective clinical assessment through a blinded panel survey.

Cephalometric analysis

In the randomized controlled trial, patients were evaluated using low-dose computed tomography (CT) scans at three points: before treatment (T0), one year after treatment (T1), and five years after treatment (T2). Cephalometric images were generated from the T0, T1 and T2 CT datasets using Planmeca Romexis software (version 6.3.0, Planmeca®, Helsinki, Finland,). The cephalograms were superimposed on the cranial base and cephalometric analysis was conducted at all time-points with the OnyxCeph ® software (version 3.6, Image Instruments GmbH, Chemnitz, Germany). The cephalometric variables used in this study are listed in table 7.2. Two independent oral and maxillofacial surgery trainees analyzed 10% of the data twice to determine the inter- and intra-observer reliability.

Virtual patient creation and panel assessment

To enable comprehensive evaluation of treatment outcomes, we created virtual patient (VP) models at the 5-year follow-up (T2). These models integrated facial scans, intraoral scans, and low-dose CT imaging, following previously described methods [36]. The VP models were used to facilitate standardized assessment across evaluators and enable detailed examination of both hard and soft tissue outcomes (Figure 7.3).

Panel survey design

A randomized presentation of 32 patients (11 FM, 11 MP, and 10 control patients, aged 12-20 years) was shown to 18 evaluators (6 maxillofacial surgeons, 6 orthodontists, and 6 laymen) using Microsoft PowerPoint ® (Version 2312, Washington, United States). The post-treatment (T2) results included 3D facial scans and virtual teeth set up. The facial scans were presented as animated 3D models. Evaluators accessed a questionnaire (Table 7.3) via QR code using Google

Forms (Alphabet Inc ®, California, United States), where they assessed treatment necessity for each case. To prevent observer bias, evaluators were not informed whether patients had received prior treatment (single-blind design).

Sample Size calculation

When this trial began, no comparative studies of these specific techniques existed. In 2010 Cevidanes et al. [3] conducted a controlled clinical trial comparing Bone Anchored Maxillary Protraction (BAMP) with Facemask and Rapid Maxillary Expansion (FM-RME), finding a mean Wits difference of 2.3 mm between groups. We pooled the standard deviations from both groups by first converting them to variances by squaring the standard deviations, then taking the average, and converting the average back to a standard deviation by taking the square root. A sample size calculation was performed for a one-sided t-test with a significance level of 0.05 and a power of 80%. This resulted in a required sample size of 12 patients per group. R version 4.1.2 was used, with the TrialSize library to calculate the sample size. We slightly overrecruited to account for potential dropouts.

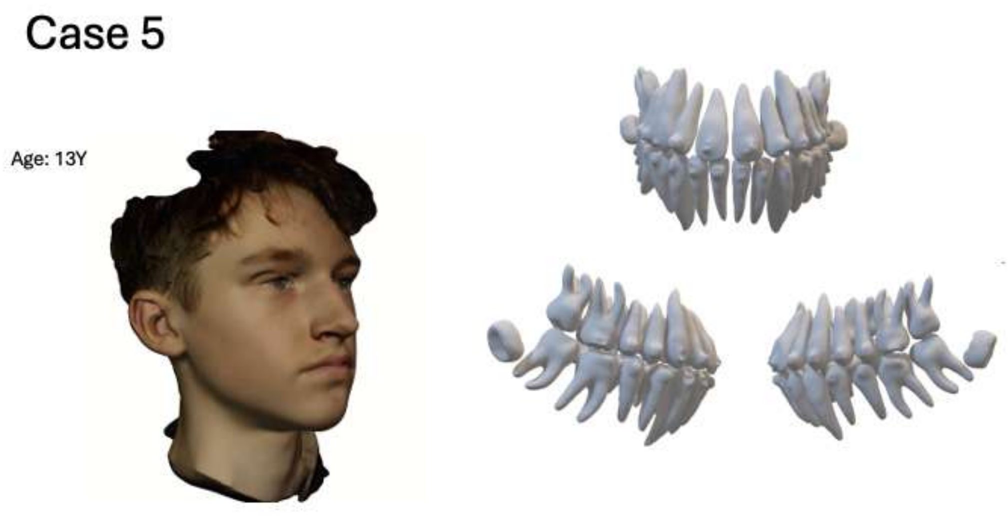


Figure 5.3*:* Virtual patient presentation for panel assessment

Table 7.3: Treatment need

1. Does this child require treatment? YES/NO
2. If yes, which kind of treatment?
a) Orthognathic surgery
b) Orthodontic: fixed appliances
c) Orthodontic: removable appliances

Patient group		Lay people	orthodontist	OMFSurgeon
overall	Tx	78%	73%	71%
	OS	47%	36%	60%
Facemask (FM)	Tx	68%	56%	51%
	OS	18%	16%	21%
Mentoplate (MP)	Tx	74%	67%	71%
	OS	29%	26%	39%
FM + MP	Tx	71%	61%	61%
	OS	23%	21%	30%

	FM	MP	FM+MP	CG
Tx	59%	71%	65%	96%
OS	19%	31%	26%	60%
avoid OS	81%	69%	74%	40%

Tx: treatment need; OS: orthognathic surgery; FM: Facemask; MP: Mentoplate.

<u>Randomization</u>

Sequence generation

The randomization sequence was generated with a 1:1 allocation ratio.

Allocation concealment

Sequentially numbered sealed, opaque envelopes.

Implementation

The envelopes containing the allocation sequence codes were given to the patient by an intermediary and opened sequentially at the time of enrollment, excluding the clinician from the process.

Blinding

Due to the nature of the trial, the operator and children could not be blinded to the treatment allocation. However, blinding was used when assessing the outcomes. This was achieved by pseudonymizing all patient data before and after treatment. The statistician analyzing the results was unaware of the group assignments.

Statistical analysis

R version 4.4.1 was used, with the irrCAC package for agreement analysis and exactRankTests for Wilcoxon signed rank test. The inter- and intra-observer reliability of cephalometric analysis was evaluated using the Intra-Class Correlation Coefficient (ICC) at a 95% confidence interval. The cephalometric data was descriptively analyzed using the median and standard deviations. Normality was tested using Shapiro-Wilkes test. The unpaired two-sided samples t-test; Wilcoxon two-sided test and Welch's two-sided t-test were employed for comparisons between two independent samples. For continuous outcomes, Pearson correlations were used to analyze relations between treatment effect and end results, for binary outcomes, point-biserial correlation was used to analyze relations between treatment effect and end results. Subjective clinical assessment was reported descriptively, and proportion of agreement was assessed. Differences in measures of agreement between observer groups were assessed with double sided t-test, whereas differences between treatment groups are reported in double sided t-test and Welch's t-test. Relations between possible predictive factors and treatment effect were fit using Pearson correlation. A p-value of < 0.05 was considered as statistically significant.

RESULTS

Measurement reliability for cephalometric analysis showed a good inter-observer (ICC:0.96- 0.99) and intra-observer reliability (ICC: 0.93 – 0.99).

Qualitative analysis of virtual patient (VP) images revealed that FM treatment was moderately more effective at preventing orthognathic surgery compared to MP treatment (19 % vs 31 % requiring surgery), with no statistical difference between both groups (p=0.19). The control group showed the highest need for surgical intervention (60 %). Survey reliability was good across observers (agreement: 0.55-0.73). Healthcare providers were slightly more conservative than laypeople in assessing treatment necessity (72% vs 78%), but this difference wasn't statistically significant. (table 7.3, table 7.4) (supporting file 4 for complete data). Cephalometric analysis at final follow-up (mean 64.5 ± 5.2 months, mean age 15.5 years), showed comparable effects with no statistical differences between both groups expect for SNO values at T2 (p= 0.02) (table 2). Mean ANB improvement was 1.58 ° (± 3.48) in the FM group compared to 1.64 ° (± 2.00) in the MP group. Similar patterns emerged in Wits measurements where FM patients showed improvement of 2.91 mm (± 2.84 mm) versus 1.36 mm (± 2.98 mm) in the MP group. Linear mixed model analysis revealed that initial SNO measurements (T0) were an independent predictor of outcomes (p=0.001), suggesting that initial severity of midface deficiency influences results more than treatment choice. Regarding the predictive cephalometric parameters, no correlation with surgical needs or final outcomes could be observed (Table 7.5). Traditional outcome measures (overjet and overbite) also failed to correlate with treatment or surgical needs. Only one factor, overbite depth indicator (ODI), showed significant correlation with both short-term (T1) and long-term (T2) ANB changes (T1: p=0.004; T2: p=0.028) and Wits changes (T1 and T2: p=0.003).

<u>Ancillary analyses</u>

No ancillary analyses were done.

<u>Harms</u>

In our MP patient group, no plate loosening was observed. Although some issues with the anchor hooks (fracture or mucosal irritation) occurred, none led to treatment cessation. No mentoplate or screws required reinsertion. Fractures were managed by additional bending of the mentoplate, while mucosal irritation was resolved through optimized oral hygiene and the application of local chlorhexidine gel.

Table 7.4: Proportion of agreement in subjective clinical assessment through blinded panel survey

proportion of agreement

Treatment need	Proportion of agreement	Confidence Interval
layperson	0.61	(0.51 - 0.72)
orthodontist	0.55	(0.47 - 0.63)
surgeon	0.60	(0.51 – 0.70)
Surgery need		
layperson	0.69	(0.58 - 0.79)
orthodontist	0.73	(0.62 - 0.84)
surgeon	0.67	(0.57 - 0.77)

proportion of agreement (95 % confidence interval)

Differences between measures of agreement

Treatment need	orthodontist	surgeon
layperson	0.30	0.89
orthodontist		0.35
Surgery need		
layperson	0.57	0.83
orthodontist		0.43

p-value: Unpaired two-sided samples t-test

Differences between treatment groups (FM vs MP)

	t-test	Welch's t-test
Treatment need	0.15	0.15
Surgery need		0.19

p-value

Table 7.5*:* Predictive cephalometric parameters.

	ANB T1-T0	ANB T2-T0	Wits T1-T0	Wits T2-T0	Need for Orthognatic Surgery
Gonial Angle	-0.15 (0.46)	-0.02 (0.94)	-0.22 (0.29)	-0.05 (0.81)	-0.09 (0.68)
ANB T0	-0.37 (0.06)	-0.54 (0.01)	-0.16 (0.46)	-0.28 (0.18)	-0.14 (0.53)
AB-MdPl	-0.17 (0.40)	-0.30 (0.16)	0.092 (0.66)	0.07 (0.75)	0.06 (0.81)
APDI	0.01 (0.98)	0.32 (0.12)	-0.16 (0.45)	0.17 (0.44)	0.08 (0.74)
ODI	-0.53 (0.00)*	-0.45 (0.03)*	-0.57 (0.00)*	-0.57 (0.00)*	-0.03 (0.89)
ANB T0T1	/	/	/	/	0.13 (0.57)
ANB T0T2	/	/	/	/	0.10 (0.67)
Wits T0T1	/	/	/	/	-0.18 (0.43)
Wits T0T2	/	/	/	/	-0.27 (0.23)
SNO T2	/	/	/	/	-0.02 (0.92)

ANB T0: ANB angle at start of treatment, AB-MdPl: AB plane -Mandibular Plane angle; APDI: Antero-posterior dysplasia index; ODI: Overbite Depth indicator; (T0). Pearson correlation coefficient (p-value, two sided alternative hypotheses); *:p-value <0.05

DISCUSSION

The decision between traditional and bone-anchored approaches for early Class III malocclusion treatment has significant implications for both clinicians and patients. Our findings challenge the growing trend toward more invasive skeletal anchorage techniques by demonstrating that FM therapy can achieve comparable long-term outcomes. Currently no evidence exists that skeletal anchorage can produce better results in the long term [4,17,19] . Previous research has established that early interceptive treatment can reduce the need for later orthognathic surgery. Mandall et al [24] found that 36% of patients who received early treatment with classic FM therapy, still required orthognathic surgery, while untreated patients were 3.5 times more likely to need surgery. A recent study examining skeletal anchorage treatment initiated at older age showed similar outcomes, with 48% of patients requiring orthognathic surgery after bone anchored maxillary protraction (BAMP) treatment (odds ratio: 0.31) [25]. Although some studies report 66-80% success in avoiding surgery [37–41], most results are limited by insufficient long-term follow-up and lack of direct comparison between treatment modalities. Our study found that the FM protocol was moderately more effective than MP, with surgery prevention rates of 81% and 69%, respectively, but not statistically significant. Inter-rater reliability scores ranged from 0.548 to 0.727, falling within or near the established benchmark of 0.61-0.80 for substantial agreement, indicating acceptable reliability of our assessment method. While 26% of all treated patients ultimately required surgery, this outcome slightly surpasses previous studies [24,25] and our results showed greater improvements in SNA (2.5° vs 0.6-1.1°) and ANB (1.58-1.64° vs 0.0-0.6°) measurements compared to these reports. The high treatment need in the control group (96 % treatment need and 60 % need for orthognathic surgery) may stem from the fact that this control group had undergone interceptive treatment for class II malocclusion, with possible suboptimal outcome. Healthcare professionals assessed the treatment necessity more conservatively than the general public, which is in line with previous research [42], but no statistical difference could be observed (Table 7.4). Among healthcare providers, orthodontists consistently rated the need for orthognathic surgery lower than oral and maxillofacial surgeons did (21 % vs 30 %), despite both groups scoring similar levels of treatment need (61 %). This difference likely stems from each specialist favoring treatment approaches they are most familiar with.

Cephalometric measurements (Table 7.2) showed no statistically significant differences at the five-year follow-up, except for SNO (p=0.02). Protraction therapy may influence the upper midface, including the zygomatic and infra-orbital regions [43]. Traditional lateral cephalograms make it difficult to assess midface skeletal structures, causing clinicians to rely primarily on the premaxilla when evaluating maxillary development. Two-dimensional cephalometric analysis, including SNO measurements, cannot fully capture the significant midface changes that improve Class III patients' concave profiles. Although correlation between SNO-angles and clinical assessment of midfacial structures has been proven [44–46]. SNO at T2 did not correlate with the need for orthognathic surgery in our study population (Table 7.5), however looking at a group level, SNO at T2 was significant higher in the FM group (p=0.02). Linear mixed model analysis showed that SNO at T0 was an independent covariate (p=0.001), indicating that patients who started with a less severe midface deficiency ended up with better results, irrespective of treatment option. It is difficult to explain the trend for better results in the FM group. Several factors may contribute to this: the more consistent force vector provided by FM therapy, coupled with the potentially beneficial effects of higher intermittent force application might better stimulate sutural growth. Additionally, the less invasive nature may allow for more natural growth adaptation. Also, myofunctional habits and patient compliance likely influenced the results, although compliance is expected to be higher in the MP group. The slightly better performance of FM therapy over MP treatment is particularly noteworthy given the greater invasiveness and cost of the latter procedure. While bone-anchored treatments are often assumed to provide better skeletal control, our findings suggest that this theoretical advantage may not translate to better clinical outcomes. While most Class III protraction therapy studies focus on cephalometric measurements, this approach may oversimplify results by focusing on measurable outcomes while overlooking aesthetic quality [47–49], especially looking at hard tissue and dental measurements [50,51]. Our findings support this concern, as we found no correlation between treatment changes (ANB and Wits) and the eventual need for orthognathic surgery (table 7.5). Significant cephalometric improvements may not necessarily indicate successful functional and aesthetic outcomes, suggesting that treatment results should be evaluated more comprehensively.

This raises important questions about patient selection and treatment predictability. The challenge of accurately forecasting individual growth patterns remains a substantial limitation in early intervention strategies. Individual patient characteristics appear to be more influential than treatment type or protraction method. Previous research has attempted to identify predictive cephalometric measurements for successful treatment outcomes, but no reliable parameters have been established yet [26,27,52]. As in most previous reports on cephalometric prediction parameters, we defined treatment outcome as obtaining a good overjet and overbite [26,28]. This simplified method of outcome reporting may not fully capture the quality of the end result, which is reflected in our study as no correlation could be found with treatment or surgical needs (table 7.5). We analyzed 5 cephalometric measurements that has been previously suggested to be of some predictive value[26] and found no correlation with treatment outcome. Neither with simplified treatment outcome reporting on overjet and overbite, nor with a more comprehensive analysis questioning treatment need at the end (table 7.5). ODI was correlated with more treatment effect (ANB and wits changes), however this did not result in a better outcome at 5-year follow-up.

Conclusion:

Our study addresses two gaps in the literature: the long-term treatment outcomes of bone-anchored treatments and the predictive value of initial cephalometric measurements. This 5-year follow-up study provides the first long-term comparative evidence between facemask and bone-anchored mentoplate protocols for early Class III malocclusion treatment. While both treatments showed some effectiveness in reducing the need for orthognathic surgery, the traditional facemask protocol demonstrated slightly better outcomes, with 81% of patients avoiding surgery compared to 69% in the mentoplate group, although statistically not significant. These findings challenge the assumption that bone-anchored treatments necessarily provide better results. Patient characteristics appear to be more influential on treatment outcomes than the chosen treatment method. Cephalometric measurements alone proved unreliable as predictive indicators. Future prediction models should incorporate multiple factors beyond just cephalometric and biomechanical data.

Several limitations should be considered when interpreting our findings. First our sample size (n=22) was relatively small, which may limit statistical power and generalizability. While this sample size is common in long-term studies due to follow-up challenges, larger multi-center trials would strengthen these findings. Second, at final follow-up (mean age 15.5 years) patients had not reached complete skeletal maturity. Additional growth changes could affect long-term outcomes. Future studies should extend follow-up through completion of growth (approximately age 18 for females and 21 for males). Third, our single-center design may limit external validity. Treatment protocols, surgical techniques, and decision-making criteria may vary across institutions. Additionally, our patient population may not represent the full spectrum of class III severity. Fourth, while attempted to control for compliance through standardized protocols, actual patient adherence to prescribed wear times (especially for FM therapy) could not be objectively measured. Fifth, our assessment of treatment need relied on subjective evaluations by professionals and laypeople. While this reflects real-world clinical decision-making, more objective criteria for determining surgical need would strengthen future research. Sixth, although an untreated Class III group would have been ideal for inclusion in the RCT, ethical constraints made this unfeasible. As an alternative, we used a control group comprising patients with Class II malocclusion who had undergone interceptive treatment. To prevent observer bias, assessors remained blinded to any previous treatment protocols for all patients. Finally, our study focused primarily on skeletal and dental measurements, with limited assessment of soft tissue changes and patient reported outcomes. Cephalometric analysis was caried out based on virtual cephalometric images derived from CT-scan performed in a supine position. To minimize positional changes of the lower jaw, a wax bite in centric relation (CR) was used during scanning, However, this measure does not eliminate the possibility of soft tissue deformation. Consequently, no soft tissue analysis was conducted on the CT images. Future research should incorporate quality of life measures and patient satisfaction data to better understand the full impact of these treatments.

Our findings have important clinical implications. First, the additional invasiveness and cost of mentoplate treatment may not be justified by improved outcomes. Facemask therapy should be considered as a first-line treatment for early Class III correction, reserving bone-anchored protocols for specific cases where traditional approaches are contraindicated, or low patient cooperation is anticipated. Second, the current findings emphasize the need for careful patient selection and realistic expectations in early Class III treatment, regardless of the chosen protocol. The results suggest that while early intervention significantly reduces surgical necessity, it should not be viewed as a guaranteed alternative to orthognathic surgery. Instead, it represents one component of a potentially multi-phase treatment approach. Patients and families must be counseled that early intervention reduces but does not eliminate the possibility of future orthognathic surgery and the ~30 % surgical rate should be discussed during treatment planning.

Other information

Registration

This Randomized Clinical trial was registered at www.ClinicalTrials.gov (ID: NCT02711111). Ethical approval has been granted by the Ethics Committee at the Ziekenhuis Oost Limburg, Belgium (EudraCT B371201629565) (13/12/2016). Ethical approval for the inclusion of the control group in the survey analysis was obtained from the Clinical Trial Center (CTC) at KU Leuven, Belgium (ID: S67723) and the Ethics Committee Research UZ/KU Leuven (EudraCT/B-nr B371201629565).

Conflicts of interest

The authors declare that they have no conflict of interest.

Data availability

The authors confirm that the data supporting the findings of this study are available within the article and its supporting materials.

REFERENCES

1. Ngan, P. W., Hagg, U., Yiu, C. & Wei, S. H. Treatment response and long-term dentofacial adaptations to maxillary expansion and protraction. *Semin Orthod* **3**, 255–264 (1997).
2. De Clerck, H. J. & Proffit, W. R. Growth modification of the face: A current perspective with emphasis on Class III treatment. *American Journal of Orthodontics and Dentofacial Orthopedics* Preprint at https://doi.org/10.1016/j.ajodo.2015.04.017 (2015).
3. Cevidanes, L., Baccetti, T., Franchi, L., McNamara, J. A. & De Clerck, H. Comparison of two protocols for maxillary protraction: bone anchors versus face mask with rapid maxillary expansion. *Angle Orthod* **80**, 799–806 (2010).
4. Rodríguez de Guzmán-Barrera, J. *et al.* Effectiveness of interceptive treatment of class III malocclusions with skeletal anchorage: A systematic review and meta-analysis. *PLoS One* **12**, e0173875 (2017).
5. Nienkemper, M., Wilmes, B., Franchi, L. & Drescher, D. Effectiveness of maxillary protraction using a hybrid hyrax-facemask combination: *A controlled clinical study*. *Angle Orthod* **85**, 764–770 (2015).
6. Wilmes, B. *et al.* The Hybrid Hyrax Distalizer, a new all-in-one appliance for rapid palatal expansion, early class III treatment and upper molar distalization. *J Orthod* **41**, s47–s53 (2014).
7. Bozkaya, E., Yüksel, A. S. & Bozkaya, S. Zygomatic miniplates for skeletal anchorage in orthopedic correction of Class III malocclusion: A controlled clinical trial. *The Korean Journal of Orthodontics* **47**, 118 (2017).
8. Şar, Ç., Şahinoğlu, Z., Özçirpici, A. A. & Uçkan, S. Dentofacial effects of skeletal anchored treatment modalities for the correction of maxillary retrognathia. *American Journal of Orthodontics and Dentofacial Orthopedics* **145**, (2014).
9. Jamilian, A. & Showkatbakhsh, R. Treatment of maxillary deficiency by miniscrew implants--a case report. *J Orthod* **37**, 56–61 (2010).
10. Kaya, D., Kocadereli, I., Kan, B. & Tasar, F. Effects of facemask treatment anchored with miniplates after alternate rapid maxillary expansions and constrictions; a pilot study. *Angle Orthod* **81**, 639–46 (2011).
11. Baek, S.-H., Kim, K.-W. & Choi, J.-Y. New treatment modality for maxillary hypoplasia in cleft patients. Protraction facemask with miniplate anchorage. *Angle Orthod* **80**, 783–91 (2010).
12. Sar, C., Arman-Özçırpıcı, A., Uçkan, S. & Yazıcı, A. C. Comparative evaluation of maxillary protraction with or without skeletal anchorage. *Am J Orthod Dentofacial Orthop* **139**, 636–49 (2011).
13. Hu, S., An, K. & Peng, Y. Comparative efficacy of the bone-anchored maxillary protraction protocols for orthopaedic treatment in skeletal Class III malocclusion: A Bayesian network meta-analysis. *Orthod Craniofac Res* **25**, 243–250 (2022).
14. YILDIRIM, G., OZBİLEN, E. O. & ÖZDEMİR, F. Retrospective 3-dimensional Evaluation of Skeletal and Dental Structures Following Treatment with Hybrid Hyrax-Mentonplate with Class III Elastics in Class III Patients with Vertical Growth Pattern: A Pilot Study. *European Journal of Research in Dentistry* **Cilt:7 Say**, 78–87 (2023).
15. Willmann, J. H., Nienkemper, M., Tarraf, N. E., Wilmes, B. & Drescher, D. Early Class III treatment with Hybrid-Hyrax – Facemask in comparison to Hybrid-Hyrax-Mentoplate – skeletal and dental outcomes. *Prog Orthod* **19**, 0–7 (2018).
16. Ergul, T. & Gulec, A. Comparison of the effectiveness of skeletal and tooth-borne protraction methods with or without alternate rapid maxillary expansion and constriction protocol in patients with Class III malocclusion. *American Journal of Orthodontics and Dentofacial Orthopedics* **article in**, (2024).
17. Cornelis, M. A., Tepedino, M., Riis, N. D. V., Niu, X. & Cattaneo, P. M. Treatment effect of bone-Anchored maxillary protraction in growing

patients compared to controls: A systematic review with meta-Analysis. *Eur J Orthod* **43**, 51–68 (2021).
18. Owens, D., Watkinson, S., Harrison, J. E., Turner, S. & Worthington, H. V. Orthodontic treatment for prominent lower front teeth (Class III malocclusion) in children (Review). *Cochrane Database of Systematic Reviews* **2024**, (2024).
19. Meyns, J., Brasil, D. M., Mazzi-Chaves, J. F., Politis, C. & Jacobs, R. The clinical outcome of skeletal anchorage in interceptive treatment (in growing patients) for class III malocclusion. *Int J Oral Maxillofac Surg* **47**, 1003–1010 (2018).
20. Lin, Y., Guo, R., Hou, L., Fu, Z. & Li, W. Stability of maxillary protraction therapy in children with Class III malocclusion: a systematic review and meta-analysis. *Clin Oral Investig* **22**, 2639–2652 (2018).
21. Woon, S. C. & Thiruvenkatachari, B. Early orthodontic treatment for Class III malocclusion: A systematic review and meta-analysis. *Am J Orthod Dentofacial Orthop* **151**, 28–52 (2017).
22. De Toffol, L., Pavoni, C., Baccetti, T., Franchi, L. & Cozza, P. Orthopedic Treatment Outcomes in Class III Malocclusion. *Angle Orthodontist* **78**, (2008).
23. Rongo, R. *et al.* Skeletal and dental effects of Class III orthopaedic treatment: a systematic review and meta-analysis. *J Oral Rehabil* (2017) doi:10.1111/joor.12495.
24. Mandall, N. *et al.* Early class III protraction facemask treatment reduces the need for orthognathic surgery: a multi-centre, two-arm parallel randomized, controlled trial. *J Orthod* **43**, 164–175 (2016).
25. Mandall, N. *et al.* The effectiveness of bone anchored maxillary protraction (BAMP) in the management of class III skeletal malocclusion in children aged 11–14 years compared with an untreated control group: A multicentre two-arm parallel randomised controlled trial. *J Orthod* (2024) doi:10.1177/14653125241255139.
26. Fudalej, P., Dragan, M. & Wedrychowska-Szulc, B. Prediction of the outcome of orthodontic treatment of Class III malocclusions-a systematic review. *Eur J Orthod* **33**, 190–197 (2011).
27. Lee, M. S., Le, V. N. T., Kim, J. G., Yang, Y. M. & Lee, D. W. Prediction Model for Future Success of Early Orthopedic Treatment of Class III Malocclusion. *Children* **10**, 1–11 (2023).
28. Choi, Y. J., Chang, J. E., Chung, C. J., Tahk, J. H. & Kim, K. H. Prediction of long-term success of orthopedic treatment in skeletal Class III malocclusions. *American Journal of Orthodontics and Dentofacial Orthopedics* **152**, 193–203 (2017).
29. Kong, H., Ngan, P., Stephen Hon-Yin Wei, Dabp. & Stephen Hon-Yin Wei, P. Early Treatment of Class III Patients To Improve Facial Aesthetics and Predict Future Growth. *Dent J* **1**, 24–30 (2004).
30. Kerr, W. J., Miller, S. & Dawber, J. E. Class III malocclusion: surgery or orthodontics? *Br J Orthod* **19**, 21–24 (1992).
31. Stellzig-Eisenhauer, A., Lux, C. J. & Schuster, G. Treatment decision in adult patients with Class III malocclusion: Orthodontic therapy or orthognathic surgery? *American Journal of Orthodontics and Dentofacial Orthopedics* **122**, 27–37 (2002).
32. Ireland, A. J. *et al.* An index of Orthognathic Functional Treatment Need (IOFTN). *J Orthod* **41**, 77–83 (2014).
33. Olkun, H. K., Borzabadi-Farahani, A. & Uçkan, S. Orthognathic surgery treatment need in a Turkish adult population: A retrospective study. *Int J Environ Res Public Health* **16**, (2019).
34. Borzabadi-Farahani, A., Olkun, H. K., Eslamian, L. & Eslamipour, F. Functional needs in orthognathic patients with different sagittal skeletal discrepancies. *Oral Surg Oral Med Oral Pathol Oral Radiol* **138**, 255–260 (2024).
35. Liou, E. J. W. & Tsai, W. C. A new protocol for maxillary protraction in cleft patients: Repetitive weekly protocol of alternate rapid maxillary expansions and constrictions. *Cleft Palate-Craniofacial Journal* **42**, 121–127 (2005).

36. Jindanil, T. *et al.* Automated orofacial virtual patient creation: A proof of concept. *J Dent* **150**, 105387 (2024).
37. Hagg, U., Tse, A., Bendeus, M. & Rabie, A. B. M. Long-term follow-up of early treatment with reverse headgear. *Eur J Orthod* **25**, 95–102 (2003).
38. Baccetti, T., Franchi, L. & McNamara, J. A. Treatment and posttreatment craniofacial changes after rapid maxillary expansion and facemask therapy. *American Journal of Orthodontics and Dentofacial Orthopedics* **118**, 404–413 (2000).
39. Wells, A. P., Sarver, D. M. & Proffit, W. R. Long-term efficacy of reverse pull headgear therapy. *Angle Orthodontist* **76**, 915–922 (2006).
40. Masucci, C. *et al.* Stability of rapid maxillary expansion and facemask therapy: A long-term controlled study. *American Journal of Orthodontics and Dentofacial Orthopedics* **140**, 493–500 (2011).
41. Gebeile-Chauty, S., Perret, M., Schott, A.-M. & Aknin, J.-J. [Early treatment of Class III: a long-term cohort study]. *Orthod Fr* **81**, 245–254 (2010).
42. Zhang, Y., Zeng, X., Cui, X., Liao, Y. & Lin, X. Facial profile esthetics and its correlation with cephalometric measurements in Class II patients before and after functional orthodontic treatment: perception of orthodontists and laypersons. *Journal of Clinical Pediatric Dentistry* (2024) doi:10.22514/jocpd.2024.051.
43. De Clerck, H. J., Cornelis, M. A., Cevidanes, L. H., Heymann, G. C. & Tulloch, C. J. F. Orthopedic traction of the maxilla with miniplates: a new perspective for treatment of midface deficiency. *J Oral Maxillofac Surg* **67**, 2123–2129 (2009).
44. Frey, S. T. New diagnostic tenet of the esthetic midface for clinical assessment of anterior malar projection. *Angle Orthodontist* **83**, 790–794 (2013).
45. Warate, P. *et al.* Comparison of Lateral Cephalograms with Photographs for Assessing Anterior Malar Prominence in Maharashtrian Population. *International Journal of Innovative Science and Research Technology (IJISRT)* **9**, 2594–2601 (2024).
46. Doshi, A. D., Shah, P., Soni, K., Solanki, A. & Mahadevia, S. Assessment of anterior malar projections using cephalometric and clinical photographs in Gujarati population. *Journal of Contemporary Orthodontics* **7**, 322–326 (2023).
47. Choki, M., Boonpratham, S. & Luppanapornlarp, S. Correlation between objective evaluation and subjective evaluation of facial profile in skeletal type ii females. *APOS Trends in Orthodontics* **11**, 223–228 (2021).
48. Knight, H. & Keith, O. Ranking facial attractiveness. *Eur J Orthod* **27**, 340–348 (2005).
49. Harrar, H., Myers, S. & Ghanem, A. M. Art or Science? An Evidence-Based Approach to Human Facial Beauty a Quantitative Analysis Towards an Informed Clinical Aesthetic Practice. *Aesthetic Plast Surg* **42**, 137–146 (2018).
50. Godinho, J., Fernandes, D., Pires, P. & Jardim, L. Cephalometric determinants of facial attractiveness: A quadratic correlation study. *American Journal of Orthodontics and Dentofacial Orthopedics* **163**, 398–406 (2023).
51. Yu, X. N. *et al.* Correlation between cephalometric measures and end-of-treatment facial attractiveness. *Journal of Craniofacial Surgery* **27**, 405–409 (2016).
52. Choi, Y. J., Chang, J. E., Chung, C. J., Tahk, J. H. & Kim, K. H. Prediction of long-term success of orthopedic treatment in skeletal Class III malocclusions. *American Journal of Orthodontics and Dentofacial Orthopedics* **152**, 193–203 (2017).

SUPPLEMENTARY MATERIAL

S1: Orthodontic protocol

1. Elastic traction
    a. Facemask:
        - Elastics: $6^{1/2}$ oz. Size 3/8” 9.5 mm HEAVY (Rhinoceros) (American Orthodontics ®)
        - Immediate full loading after placement of hybrid hyrax
        - First 6 months (or until an overjet of 2 mm or more is achieved): elastic traction for 12–14 h a day overnight.
        - Following 6 months: elastic traction only during sleep
        - After 12 months: No elastic traction

    b. Mentoplate
        - Elastics: $6^{1/2}$ oz. Size 3/16” 4.8 mm HEAVY (Tortoise) (American Orthodontics ®)
        - Full loading 1 week after mentoplate placement (no gradual build up)
        - First 6 months (or until an overjet of 2 mm or more is achieved): continuous elastic traction (included during meals)
        - Following 6 months: elastic traction only during sleep
        - After 12 months: No elastic traction

2. Fixed appliances

   - No fixed appliances during the first 12 months (more specific no fixed appliances till the first follow-up CT scan was taken)
   - MBT prescription with Empower2 selfligating bracket (American Orthodontics ®)
   - Change of wire every 6- 8 weeks (12 weeks in case of square wires)
   - Sequence:

     .014 niti (.012 niti in case of severe misalignment)

     .018 niti

     .020 x.020 niti

     .020 x .020 SS

     .019 x .022 SS (torque control)

     .019 x 0.22 Beta-titanium (finishing, artistic steps)

     Natural arch I

3. Occlusal disarticulation

   Only when necessary: clear overlay in the lower jaw (1 mm thickness) (DURAN ® 1.0 x125mm, Scheu ®).

4. Oral hygiene instructions

   When placing the Hybrid Hyrax (H-H), patients are instructed to brush the PSM screws twice a day with a regular toothbrush to prevent gingival overgrowth. The space between the H-H and the palate is cleaned using a 1.3 conical interproximal brush (Dentaid ®). In cases where the hooks on the mentoplate cause minor injuries, they are shortened or adjusted in the mouth with a three-prong plier. To prevent skin irritation on the chin from the facemask (FM), we prescribe Homeoplasmine ointment, Boiron ®. Oral hygiene instructions are provided by an orthodontic assistant at the time of fixed appliance placement, using Dentaid ® orthodontic care kit (Vitis Orthodontic toothpaste, Vitis Orthodontic mouth rinse, wax, interdental brushes, and a Vitis toothbrush). At every follow-up appointment, oral hygiene is evaluated and, if needed, further guidance is given.

5. Removal of Hybrid Hyrax and mentoplate

   The hybrid hyrax device is removed when fixed appliances are in place and a satisfactory overjet overcorrection (at least 2 mm) is achieved. Removal of the mentoplate often coincides with the extraction of wisdom teeth, if indicated, with the timing determined by the developmental stage of those teeth.

S2: FM values. Cephalometric values of all patients at all time-points (T0, T1, T2)

		Sagittal					predictive factors					Quality of end result
		SNA°	SNB°	ANB°	Wits	SNO	Ar-Go-Me	ANB T0	AB-MdPl°	APDI	ODI	OJ/OB
FM1	T0	80,8	79,6	1,2	-4	59	120	1,2	70,3	86,6	68,1	
	T1	82,7	79	3,7	-2	60						
	T2	81,9	80	2	-3	61						Good
FM2	T0	76,2	81,8	-5,6	-9	56	113	-5,6	64,1	90,5	52,6	
	T1	81,8	80,8	1	-3	60						
	T2	83	81	2	-1	60						Good
FM3	T0	80,9	80,4	0,4	-5	60	119	0,4	66	83	59,5	
	T1	85,7	80,1	5,6	1	60						
	T2	85,5	81,7	3,7	-2	61						Good
FM4	T0	77,8	77,5	0,3	-5	54	125	0,3	70	83,6	66,4	
	T1	76,7	74,4	2,3	-1	54						
	T2	76,4	77,4	-1	-4	55						Good
FM5	T0	79,5	78,9	0,6	-7	58	125	0,6	63,4	93	60,6	
	T1	81,1	80,7	0,4	-4	60						
	T2	80,8	83	-2,2	-7	60						Good
FM6	T0	82,1	81,5	0,5	-6	54	121	0,5	65,9	89,1	62,2	
	T1	83	81,1	1,9	-4	57						
	T2	85	86,8	-1,8	-5	57						Good
FM7	T0	76,5	76	0,6	-6	50	128	0,6	61,1	84,5	55,6	
	T1	83,4	75,8	7,6	3	55						
	T2	82,2	76,8	5,4	0	55						Good
FM8	T0	78,3	78,8	-0,6	-7	52	131	-0,6	65,3	92,8	60,1	
	T1	80,1	78,6	1,5	-5	55						
	T2	82,4	77	5,4	0	55						Bad
FM9	T0	82,6	83,4	-0,8	-6	54	137	-0,8	62,8	91,1	55,8	
	T1	83,8	80,4	3,4	-1	56						
	T2	80,7	80	0,7	-4	56						Good
FM10	T0	76,4	80,6	-4,2	-8	55	124	-4,2	61,9	97,5	57,3	
	T1	81	80,6	0,5	-2	59						
	T2	81,8	84,9	-3	-5	58						Bad
FM11	T0	78,8	79,1	-0,3	-3	50	126	-0,3	68,2	87,4	63,5	
	T1	79,9	79,7	0,2	-2	54						
	T2	78,7	80,4	-1,7	-3	54						Good

S3: MP values. Cephalometric values of all patients at all time-points (T0, T1, T2)

		Sagittal					predictive factors					Quality of end result
		SNA°	SNB°	ANB°	Wits	SNO	Ar-Go-Me	ANB T0	AB-MdPl°	APDI	ODI	OJ/ OB
MP1	T0	76,1	76,1	0	-5	52	122	0	69,1	87,2	67,5	
	T1	74,9	74,2	0,7	-4,7	50						
	T2	75,6	76,3	-0,8	-3	45						Bad
MP2	T0	70,3	68,9	1,4	-10	49	131	1,4	60,2	80,8	59	
	T1	70,8	67,4	3,5	-4	45						
	T2	68,4	67,9	0,5	-9	50						Good
MP3	T0	80	80	0	-7	47	132	0	60,2	91,6	62,9	
	T1	83,5	82	1,6	-8	51						
	T2	83,2	81,8	1,5	-5	51						Good
MP4	T0	72,9	72,5	0,5	-2	55	124	0,5	68	83	62,8	
	T1	78,3	75,8	2,5	-1	50						
	T2	76,2	75	1,2	-3	50						Good
MP5	T0	80,1	81,3	-1,1	-5	54	126	-1,1	64,6	89,2	58,3	
	T1	82	80,6	1,4	-2	54						
	T2	82	81,9	0,1	-6	55						Good
MP6	T0	79,6	78,9	0,7	-4	51	134	0,7	65.3	87,8	65,9	
	T1	81,2	77,5	3,7	-2	54						
	T2	81,2	77,6	3,6	1	51						Good
MP7	T0	79,3	80	-0,8	-2	51	132	-0,8	69.4	88,1	70,2	
	T1	81,3	78,7	2,6	0	55						
	T2	82,3	83,7	-1,4	-6	55						Bad
MP8	T0	79,2	80	-0,8	-4	54	120	-0,8	71.5	88,7	65,7	
	T1	81,4	78,2	3,2	0	54						
	T2	82,2	81,5	0,7	-4	55						Good
MP9	T0	77,3	79,4	-2,1	-7	55	132	-2,1	61	100,9	71,2	
	T1	76,4	78,3	-1,9	-7	55						
	T2	80,4	78,6	1,8	-5	55						Good
MP10	T0	79,1	83,2	-4,1	-8	54	127	-4,1	55.4	104,7	57,9	
	T1	84,1	83,2	0,9	-4	59						
	T2	85,9	85,2	0,7	-6	60						Good
MP11	T0	83,3	84,7	-1,4	-8	59	134	-1,4	58.2	91,8	51,4	
	T1	85,8	83,2	2,5	-2	59						
	T2	87,4	84,9	2,4	-1	60						Good

S4: Treatment need per patient for the Mentoplate group. Result of survey analysis per patient. T: treatment need, S: need for orthognathic surgery, L1: lay-person, O1: orthodontist, S1: surgeon, 1: yes, 0: no

Patient		L1	L2	L3	L4	L5	L6	O1	O2	O3	O4	O5	O6	S1	S2	S3	S4	S5	S6
MP1	**T**	0	1	0	1	0	0	0	0	1	0	1	0	1	0	1	1	0	1
	S	0	1	0	1	0	0	0	0	1	0	1	0	1	0	1	1	0	1
MP2	**T**	0	1	0	1	1	0	0	1	1	1	1	0	1	0	1	1	1	1
	S	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0
MP3	**T**	1	1	0	1	1	1	1	0	1	1	1	0	0	0	1	1	0	0
	S	0	1	0	1	0	0	1	0	1	1	1	0	0	0	1	1	0	0
MP4	**T**	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	0	1	0
	S	0	1	0	0	0	0	1	0	0	0	0	0	0	1	0	0	1	0
MP5	**T**	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	S	1	0	0	1	1	1	0	0	1	1	1	1	1	1	1	1	1	0
MP6	**T**	0	1	1	1	1	0	1	0	1	1	1	0	1	0	1	1	1	1
	S	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0
MP7	**T**	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	S	0	1	0	0	0	1	1	1	0	0	0	0	1	1	1	1	1	1
MP8	**T**	0	0	1	1	1	1	1	1	1	0	0	0	0	0	1	1	0	1
	S	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
MP9	**T**	1	0	1	1	0	1	0	0	1	0	0	0	0	0	0	0	0	1
	S	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
MP10	**T**	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1
	S	0	0	0	0	1	1	1	1	1	0	1	0	0	1	1	0	1	1
MP11	**T**	0	0	0	1	1	1	1	1	1	1	1	0	1	1	1	1	0	1
	S	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0

S4: Treatment need per patient for the Facemask group. Result of survey analysis per patient. T: treatment need, S: need for orthognathic surgery, L1: lay-person, O1: orthodontist, S1: surgeon, 1: yes, 0: no

Patient		L1	L2	L3	L4	L5	L6	O1	O2	O3	O4	O5	O6	S1	S2	S3	S4	S5	S6
FM1	**T**	0	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	0	1
	S	0	1	1	0	0	1	0	1	0	0	0	0	0	1	0	0	0	0
FM2	**T**	0	1	1	1	1	1	0	1	1	0	1	1	1	0	1	0	1	1
	S	0	0	1	1	1	0	0	0	0	0	0	1	1	0	1	0	0	0
FM3	**T**	1	1	1	1	1	1	0	0	1	1	1	1	1	0	1	0	1	0
	S	0	0	0	1	0	1	0	0	0	0	1	1	1	0	1	0	1	0
FM4	**T**	1	1	0	1	0	1	0	1	1	0	1	0	0	0	0	1	0	1
	S	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
FM5	**T**	1	1	1	0	0	1	0	1	1	0	0	0	0	0	1	0	0	1
	S	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	1
FM6	**T**	1	1	1	1	0	1	1	1	1	1	0	0	0	1	1	1	1	0
	S	0	0	0	0	0	0	1	0	1	0	0	0	0	1	0	0	0	0
FM7	**T**	1	1	1	1	0	0	0	1	1	0	0	0	0	0	0	0	0	0
	S	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
FM8	**T**	0	1	1	1	0	0	1	1	1	1	1	0	0	0	1	1	1	1
	S	0	0	0	1	0	0	1	0	1	0	1	0	0	0	0	0	1	0
FM9	**T**	0	1	1	0	0	0	0	0	1	1	1	0	0	1	1	0	1	1
	S	0	0	1	0	0	0	0	0	0	0	0	0	0	1	1	0	1	0
FM10	**T**	1	1	0	1	0	0	0	1	1	0	0	0	0	0	1	0	0	1
	S	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
FM11	**T**	1	0	1	1	1	0	1	1	1	0	0	0	1	0	1	1	1	1
	S	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

S5: Treatment need per patient for the Control group. Result of survey analysis per patient. T: treatment need, S: need for orthognathic surgery, L1: lay-person, O1: orthodontist, S1: surgeon, 1: yes, 0: no

Patient		L1	L2	L3	L4	L5	L6	O1	O2	O3	O4	O5	O6	S1	S2	S3	S4	S5	S6
CG1	T	1	1	1	0	1	0	1	1	1	1	1	1	1	1	0	1	1	1
	S	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1
CG2	T	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	S	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	1	1	1
CG3	T	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	S	1	1	0	0	1	1	1	1	1	0	1	0	1	1	1	1	1	1
CG4	T	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	S	0	1	1	1	1	1	0	1	1	0	1	1	1	1	0	1	1	1
CG5	T	1	1	0	1	1	0	1	1	1	1	1	1	1	1	1	1	0	1
	S	1	1	0	0	1	0	1	0	1	0	0	1	1	1	0	1	0	1
CG6	T	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1
	S	1	1	1	1	0	0	1	0	1	0	1	1	1	1	1	1	0	1
CG7	T	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	S	1	1	0	0	0	1	1	0	0	0	0	0	1	0	0	1	1	0
CG8	T	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1
	S	0	1	1	1	0	1	0	0	0	0	0	0	1	1	0	0	0	1
CG9	T	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	S	0	1	1	1	1	1	0	0	0	0	0	0	1	1	0	0	1	1
CG10	T	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	S	1	1	1	1	0	1	1	0	0	0	0	1	1	1	0	0	1	1

CHAPTER 8

Three-Dimensional analysis for predicting class III malocclusion treatment effect.

This chapter is based on the following manuscript.

Meyns J., Vertenten W., Shujaat S., Van Cauter S., Politis C., Vander Sloten J., Jacobs R. Evaluating the Predictive Potential of Patient-Specific Biomechanical Models in Class III Protraction Therapy**.** *Under Review with Clinical Oral invest.*

.

ABSTRACT

Introduction:

Predicting treatment outcomes in skeletal Class III using maxillary protraction therapy in growing individuals remains challenging. Although finite element analysis (FEA) helps study biomechanics and plan orthodontic treatment, its use in Class III protraction has mainly evaluated appliance designs rather than patient-specific anatomy. Furthermore, its predictive accuracy has not been validated.

Materials and Methods:

Ten patients with skeletal Class III malocclusion received either facemask or mentoplate treatment. CT scans of 4 patients were used to construct simplified finite element models. To assess model accuracy, predicted upper jaw deformations were compared with one-year treatment outcomes from six additional patients.

Results:

While stress patterns in the upper jaw differed between both treatments, these variations did not affect maxillary deformation. Patient-specific geometrical factors had a more significant impact on deformation than treatment type. Our simplified FEM aligned with previous class III protraction models but underestimated clinical outcomes. FEM-predicted maxillary changes (0.110-0.509 mm, mean: 0.352 ± 0.12 mm) were roughly one-tenth of actual changes (0.429-3.116 mm, mean: 1.612 ± 0.64 mm), with no significant correlation.

Conclusions:

Current FEM approaches, while useful for understanding force distribution, cannot reliably predict clinical outcomes in growing Class III patients. The consistent discrepancy between predicted and actual deformations suggests that successful prediction models must incorporate biological and growth factors beyond pure biomechanics.

Clinical Relevance:

Simplified biomechanical models are insufficient for treatment planning in Maxillary protraction therapy. To accurately predict treatment outcomes, we need validated models that incorporate biological markers, growth patterns and individual tissue responses.

INTRODUCTION

Treating skeletal Class III malocclusion in growing individuals is a complex challenge in orthodontics, largely due to the unpredictable growth potential of the maxilla and the possibility of unfavorable mandibular growth. Predicting the magnitude and timing of skeletal growth remains difficult, complicating the decision-making process for early intervention. Moreover, the debate surrounding the eligibility criteria for early Class III treatment underscores the need for refined diagnostic and prognostic tools [1–4].

Facemask (FM) therapy, often combined with rapid palatal expansion (RPE), is a common approach to managing Class III malocclusion [5]. However, the effectiveness of such treatments depends on how forces are transmitted to the jaw. Force application through dental structures (tooth-borne, TB) generally produce limited skeletal effects. Skeletal anchorage (SA) devices, such as mentoplate and palatal screws (including Hybrid Hyrax), may offer better skeletal results and vertical control, especially in high angle patients [6–9] . However, despite their increasing use, there is no clear consensus on when and how to use these invasive devices. Questions remain about optimal treatment age, force levels, and whether these devices improve outcomes compared to conventional methods [10–13].

Even successful initial protraction treatments can deteriorate over time, resulting in poor occlusion or facial aesthetics as patients mature [4]. The key challenge is identifying which patients will maintain positive long-term outcomes from early intervention versus those who should wait for skeletal maturity and possible orthognathic surgery. While predictive models using 2D cephalometric and CBCT measurements exist, most are based on retrospective studies without proper validation [14–16]. New approaches combining these measurements with initial treatment response show promise [17], but their predictive accuracy remains uncertain [14].

Research on maxillary protraction has evolved from basic models (wax, elastic, and dry skulls) to sophisticated 3D imaging and finite element (FE) modeling. While early studies established fundamental concepts like centers of resistance and rotation [18–24], modern FE analysis has enhanced our understanding of force distribution, particularly with skeletal anchorage (SA) techniques [25–28]. However, current FE studies reporting on SA techniques have limitations: they show conflicting results regarding skeletal effects and vertical control [26,27], rarely address mandibular deformation [25–27,29], and typically focus on appliance design rather than patient-specific factors like anatomy. While FEM has shown promise in orthodontic applications, a critical gap exists: no studies have validated these models against actual clinical outcomes in maxillary protraction therapy. This validation step is essential, as treatment success depends not just on biomechanical forces, but on complex biological responses that may not be captured by current modeling approaches. Understanding whether FEM can reliably predict treatment outcomes would either validate current biomechanical approaches to treatment planning or reveal the need for more sophisticated predictive tools. This study aimed to determine whether patient-specific finite element models could predict actual treatment outcomes using maxillary protraction therapy in growing individuals with skeletal class III. Using image data from a randomized controlled trial, we tested two hypotheses: (1) that simplified FEM could accurately predict stress distribution and deformation patterns corresponding to actual treatment effects, and (2) that different treatment techniques (FM vs MP) would produce distinct patterns of skeletal deformation, potentially leading to improved treatment effect. This represents the first direct comparison between FEM predictions and clinical outcomes in maxillary protraction therapy.

MATERIALS AND METHODS

Subjects

This study analyzed biomechanical models from CT scans of ten Caucasian patients (5 female, 5 male, aged 7-11 years) with Class III skeletal malocclusion. The patients participated in a randomized controlled trial (EudraCT B371201629565) comparing Facemask (FM) (Figure 8.1) and Mentoplate (MP) (Figure 8.2) treatments, with follow-up periods of 9-14 months. All patients received a Hybrid Hyrax apparatus (HH) assembled with 2 mini-screws in the anterior palate and an expansion screw attached to first molar bands (Figure 8.1 and 8.2). Alternate

Rapid Maxillary Expansion and Constriction (Alt-RAMEC) protocol was employed [30]. Elastic forces in the FM group: 360-400g force per side, worn 12-14 hours daily and in the MP group: 185g force per side, worn continuously. To develop a simplified Finite Element Model (FEM), we randomly selected two patients from each treatment group. The model was then tested on six additional patients (3 FM, 3 MP) to evaluate its predictive capabilities for treatment outcomes.

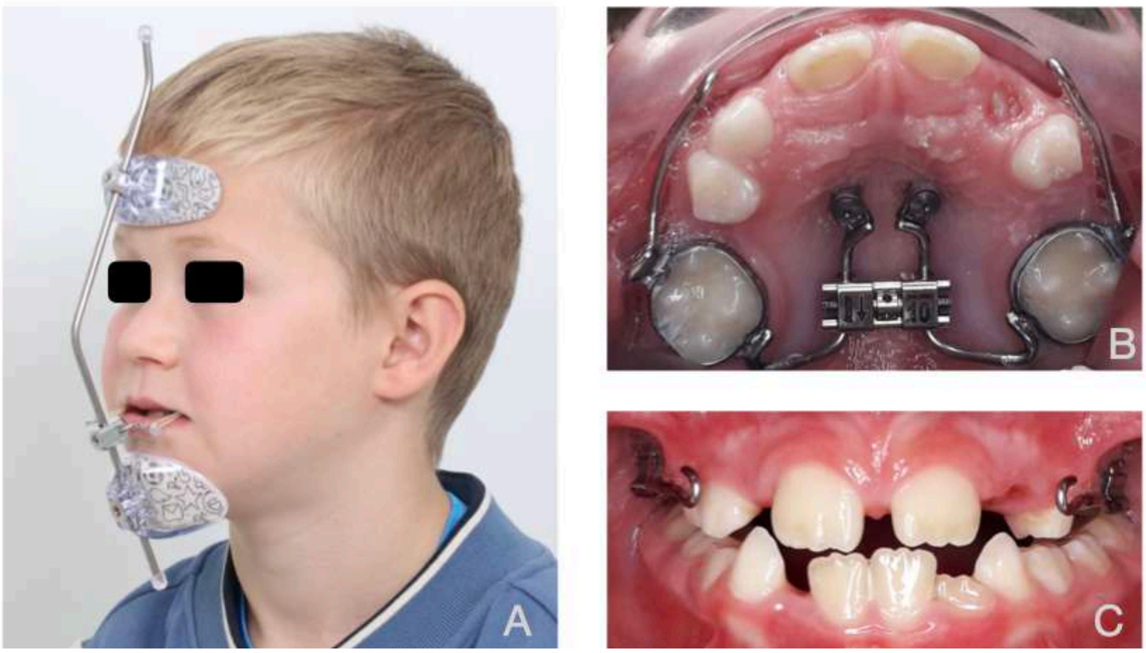


Figure 8.1: Facemask

A. Extra-oral view.
B. Occlusal view (Hybrid Hyrax).
C. Intra-oral view

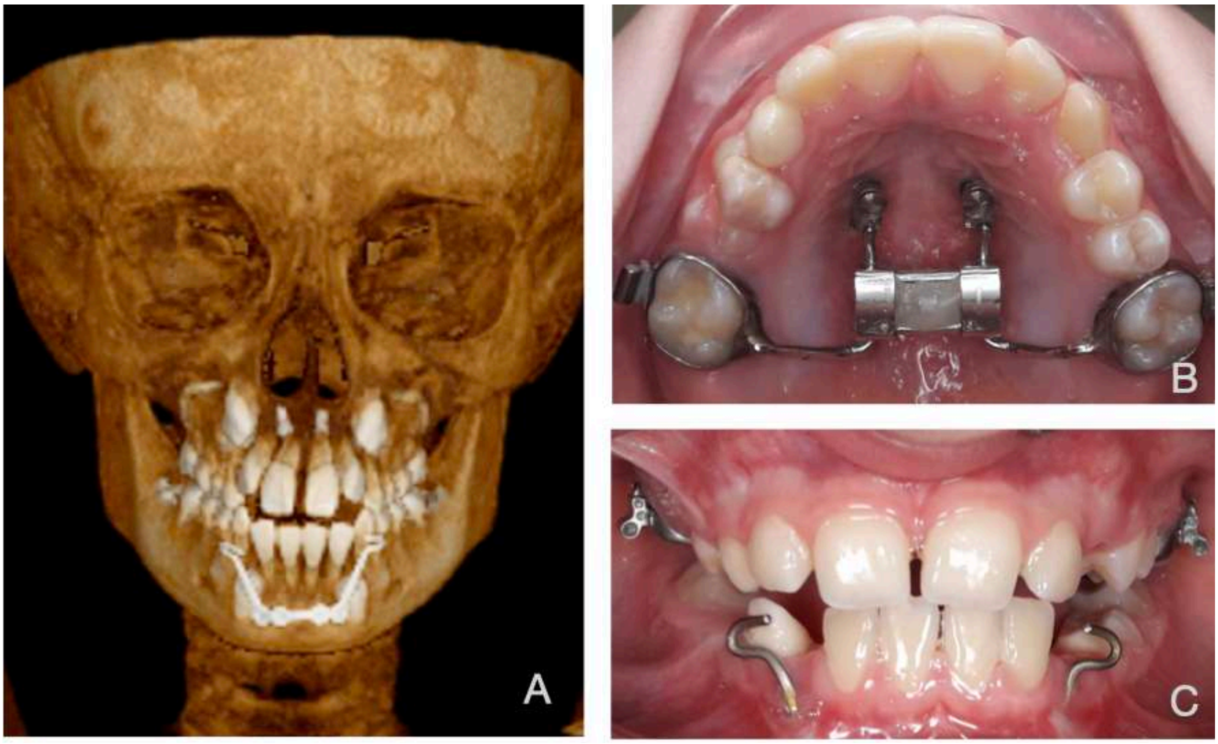


Figure 8.2: Mentoplate
A. 3D volumetric frontal view (derived from CT data)
B. Occlusal view (Hybrid Hyrax)
C. Intra-oral view with the hooks of the mentoplate clearly visible

Creating a patient specific 3D FE model

The CT scans were taken at the start of the treatment (T0) and saved in Digital Imaging and Communications in Medicine (DICOM) format. CT scans were performed on a Siemens Somatom Force (Siemens ®, Erlangen, Germany) with a slice thickness of 0.6 mm, 50 mA and 150 kV and a scan time of 2.04 sec. These files were imported into Mimics® software (version 20.0, Materialise®, Leuven, Belgium), which was used to segment the craniomaxillofacial structures. This segmentation excluded regions that were not critical to the analysis, such as posterior midface, and skull. Exclusion of these structures enabled us to focus on the maxillary and mandibular bone structures, reducing computational complexity and improving processing efficiency (Figure 8.3). The teeth were also removed since forces were transferred through a bone-anchored device (Hybrid Hyrax), which has been proven to produce good skeletal anchorage with minimal dento-alveolar effect [9,26]. The periodontal ligament was not simulated, based on a previous study suggesting that modeling the periodontal ligament in finite element analyses of skulls can be ignored if the values of stress and strain in the alveolar region are not required [31]. Finally, the superior portion of the alveolar process was excluded because significant remodeling occurs in this region during tooth eruption, which could interfere with accurate comparisons to the one-year follow-up scan. After segmentation, the 3D model was transferred to 3-Matic software (Materialise®, Leuven, Belgium) for meshing and refinement. A surface mesh was generated using specific edge lengths tailored to the anatomical features of the structures: 1 mm for the maxilla and 2 mm for the mandible. These sizes were chosen based on previous studies [26] and to balance accuracy and computational efficiency, as the maxilla's finer bone structures required higher resolution, while the mandible's thicker and less complex geometry allowed for a coarser mesh without compromising accuracy. Different triangle edge lengths were used to maintain anatomical accuracy. The meshing process also involved ensuring that the surface mesh was free from elements with poor computational properties, such as sharp internal angles. Following this, a uniform volume mesh type was applied to both jaws for consistency during finite element analysis (FEA). The final 3D meshed FE models, depicted in Figure 8.3C, represent the maxillary and mandibular structures in detail, for further processing.

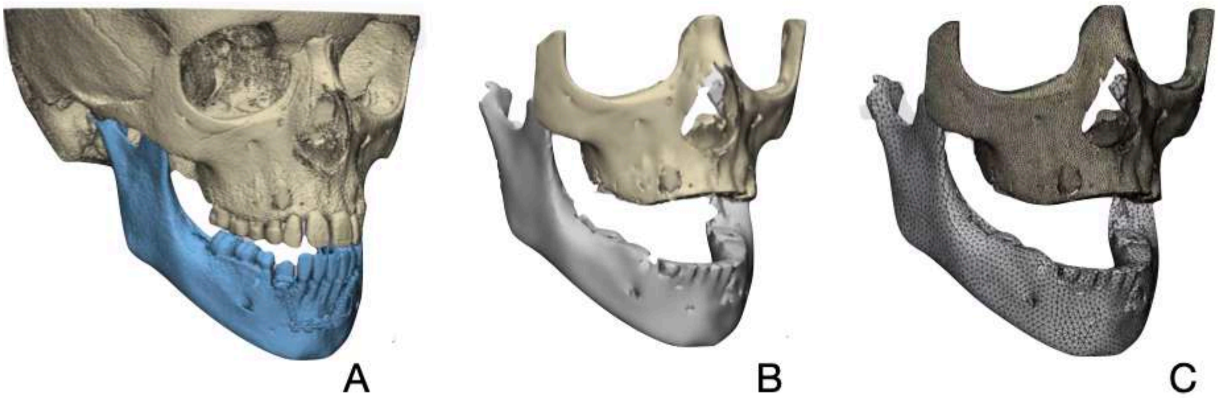


Figure 8.3: (A) Original DICOM dataset model. (B) Modified model with teeth, superior part of alveolar process, posterior midface, cranial base and skull region removed. (C) Finite element model showing detailed anatomical representation, with 2 mm mesh for mandible and 1 mm mesh for maxilla.

Finite element Model (FEM)

FEA was conducted using Abaqus® software (Dassault Systèmes®, France) to evaluate the biomechanical behavior of the patient-specific FE models. The models incorporated forces with calculated magnitudes and orientations, as well as boundary conditions. This analysis provided insights into the stress distributions, deformation patterns, and the resulting deformed geometries of the maxilla and mandible under simulated treatment conditions. For this simplified FEM, the maxilla and mandible were modeled as uniform bone structures with isotropic and elastic material properties to ensure computational efficiency while maintaining physiological relevance. The assigned material properties were based on previous studies [25–28]. The maxilla was assigned a Young's modulus of 700 MPa and a Poisson's ratio of 0.3, representing its primarily trabecular bone composition, which is softer and more porous. In contrast, the mandible was assigned a Young's modulus of 1000 MPa and a Poisson's ratio of 0.3, reflecting its denser, cortical bone structure, which contributes to its increased stiffness.

Boundary conditions

Boundary conditions for the upper jaw were applied to the infra-orbital rim (Figure 8.4), a region experimentally shown to remain stable during growth and treatment [32]. This area experiences minimal remodeling, making it an ideal reference point for constraining movement in the FEA. By fixing displacements in all three spatial directions at selected nodes, while allowing rotation, the model accurately reflects the biomechanical stability of this region. For the lower jaw, identifying suitable boundary condition locations is more complex due to the dynamic remodeling of various regions during growth. While the anterior chin and internal symphysis have been considered stable and reliable for voxel-based superimposition in growing patients [33], applying boundary conditions at these locations can overly constrain the model. The combination of these areas' higher Young’s modulus and boundary constraints inhibits realistic deformation when treatment forces are applied. Similarly, the condylar region is excluded as it undergoes significant remodeling during growth and treatment, making it unsuitable as a stable reference [34]. To address this issue, a three-dimensional volumetric part-comparison analysis was performed on patient data of 4 patients obtained in our RCT to identify stable regions in the lower jaw during one year treatment follow-up. This analysis revealed that the angle of the mandible exhibited minimal deformation across these patients, establishing it as a relatively stable area suitable for applying boundary conditions. Three nodes were fixed at each mandibular angle to achieve optimal model stability while allowing deformation. This approach balances the mandible's high stiffness (Young's Modulus) with realistic movement, as more constraints would prevent deformation and fewer would create instability (Figure 8.4).

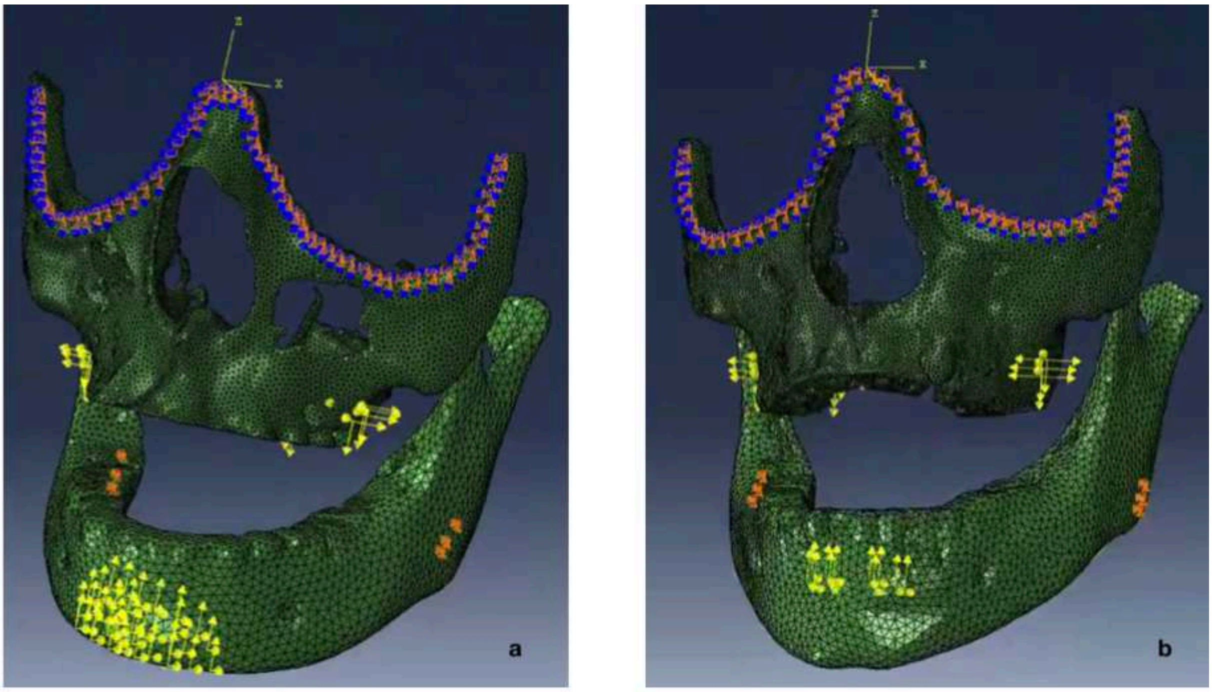


Figure 8.4: Two finite element models show maxillary protraction using: (a) Facemask and (b) Mentoplate. Yellow markers indicate force application points, while orange markers show boundary conditions at the infra-orbital rim (upper jaw) and mandibular angle (lower jaw).

Magnitude and vector of the forces

MP therapy uses low-force elastics that generate approximately 200g of force per side [8,35,36] and are worn continuously (24/7). Using 3-Matic software, the precise direction of the force vector can be calculated for each patient by analyzing the line between the MP's attachment point on the mandible and the molar anchor points. This patient-specific calculation ensures accurate modeling of force orientation in FE simulations. In contrast, FM therapy requires higher forces elastics that generate approximately 400 g per side and are worn 12 – 14 hours daily. The vector of force is positioned at an angle of 25–30° to the occlusal plane [1,37,38]. The orientation of these elastics is determined by first measuring the occlusal plane angle, then adding 25–30°. Both MP and FM therapies integrate Alt-RAMEC using a HH expander, which is equipped with dual palatal mini-screws. This device generates approximately 2500 g of force during palatal expansion [39–41], which facilitates craniofacial suture activation and enhances the treatment effects of both MP and FM therapies.

Force simulation

The forces acting on the upper and lower jaws were applied to the FE model through node sets to ensure accurate simulation of treatment forces (Figure 8.4). For the upper jaw, node selection was guided by the design of the HH device. Two primary sets of nodes were chosen to represent the distribution of expansion and elastic forces. The first set was located in the apical region of the first molars, simulating the forces transmitted through the molars. The second set included nodes in the region of the two screws in the anterior palate, which modeled the effects of palatal expansion. This configuration allowed for realistic simulation of both FM and MP therapy forces in the upper jaw.

In the lower jaw, the method of force application differed between FM and MP therapies. For FM therapy, 43 nodes were selected within the chin-cup contact area (Figure 8.4a). These nodes were distributed to cover the interaction zone where the FM applies pressure to the mandible, ensuring that the force transmission was realistically simulated. For MP therapy, each screw of the MP was represented by six nodes—three on the external surface and three internally within the mandible (Figure 8.4b). This arrangement was designed to accurately model the dispersive effect of forces as they propagate through the bone tissue surrounding the screws.

The models incorporated realistic forces, with MP therapy requiring twice the elastic wear time of FM therapy. The number of deformation cycles was adjusted accordingly for each treatment to match actual clinical usage patterns. To capture these variations, the FM models were subjected to 5 deformation cycles, while the MP models underwent 10 cycles. Abaqus software enabled the iterative reapplication of forces to the already deformed geometry of the models, further enhancing the patient-specific accuracy of the FEA. This approach ensured that the simulation realistically represented the cumulative deformation and stress patterns corresponding to each treatment protocol.

The differences between the deformed and baseline models were analyzed using part comparison analysis. This technique produced color-coded maps that visualized the extent of deformation across various regions of the jaw structures. By incorporating these methods, the simulation captured the biomechanical behavior of craniofacial structures under treatment, providing insights into force distribution and the resulting deformations with high precision. Supplementary file 1 provides more details on node sets and forces applied on these nodes.

Actual treatment effect

The baseline (T0) and one-year follow-up (T1) CT datasets were imported into Amira® software (version 2019.1, Thermo Fischer Scientific®, Merignac, France) in DICOM format to analyze skeletal changes over the treatment period. Using volume rendering, the datasets were visualized in 3D to enable precise identification of structural differences (Figure 8.5). A rigid voxel-based registration was performed with mutual information as the alignment metric, ensuring accurate superimposition of the datasets [42,43]. The T1 dataset was registered to T0 using stable anatomical landmarks: the inferior orbital rim for the maxilla and both the external oblique ridge and mandibular angle for the mandible. The inferior orbital rim's stability is well-documented in literature [32], while our previous analysis confirmed the stability of the mandibular landmarks during growth. Following registration, the T0 and T1 datasets were imported into Mimics® software (version 20.0, Materialise®, Leuven, Belgium) for segmentation. A semi-automatic thresholding approach, refined with manual adjustments, was employed to construct high-resolution 3D volumetric surface models of the maxilla and mandible. These models were then exported in STL format (Figure 8.5), preserving the geometric fidelity required for further analysis.
The STL models were subsequently transferred to 3-Matic® software (version 14.0, Materialise®, Leuven, Belgium) for part comparison analysis. This process calculated the mean differences between the T0 and T1 datasets, quantifying treatment-induced changes in the skeletal structures. The results were visualized as a color-coded map (Figure 8.5), with different colors representing the magnitude and distribution of deformation.

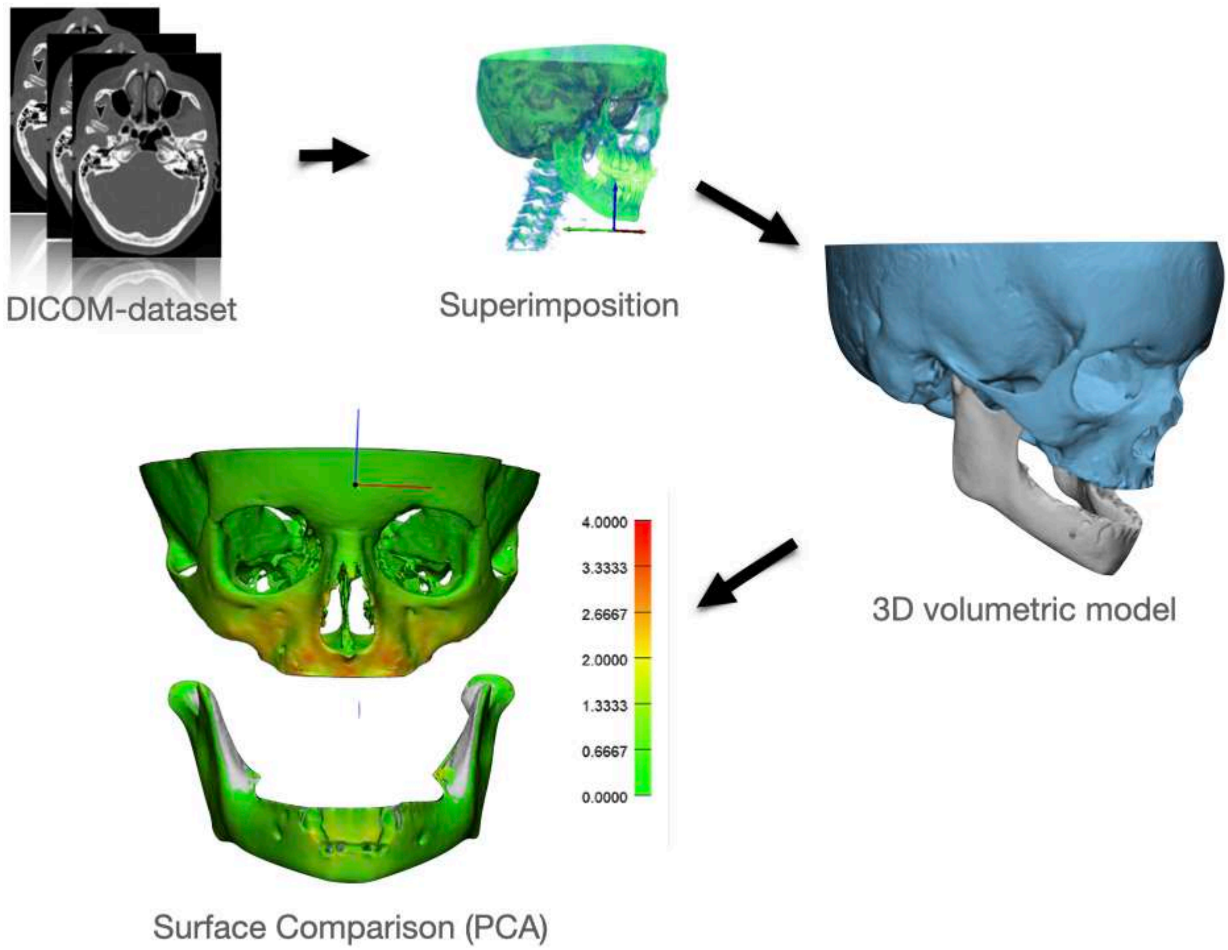


Figure 8.5: Workflow Part Comparison Analysis: Both datasets are super-imposed (Amira ®), Segmentation is performed in Mimics ® (semi-automatic) and exported in a 3D volumetric model (stl). Surface comparison is done in 3-Matic ® and color-coded images are generated.

Comparing modeled deformation with actual deformation

We evaluated the accuracy of our FEM by comparing predicted (PCAmD) and actual (PCAaD) deformations using both visual and quantitative methods. Color-coded maps illustrated deformation patterns, though direct comparisons were challenging since PCAmD values were notably smaller than PCAaD. Initial analysis of maxillary deformation in 4 FEM cases showed promising results, but mandibular comparisons were not possible due to model limitations. We expanded the study with 6 additional patients, focusing on maxillary deformation and using five anatomical landmarks per patient for quantitative analysis (Figure 8.6). The correlation between PCAmD and PCAaD values at these landmarks were analyzed.

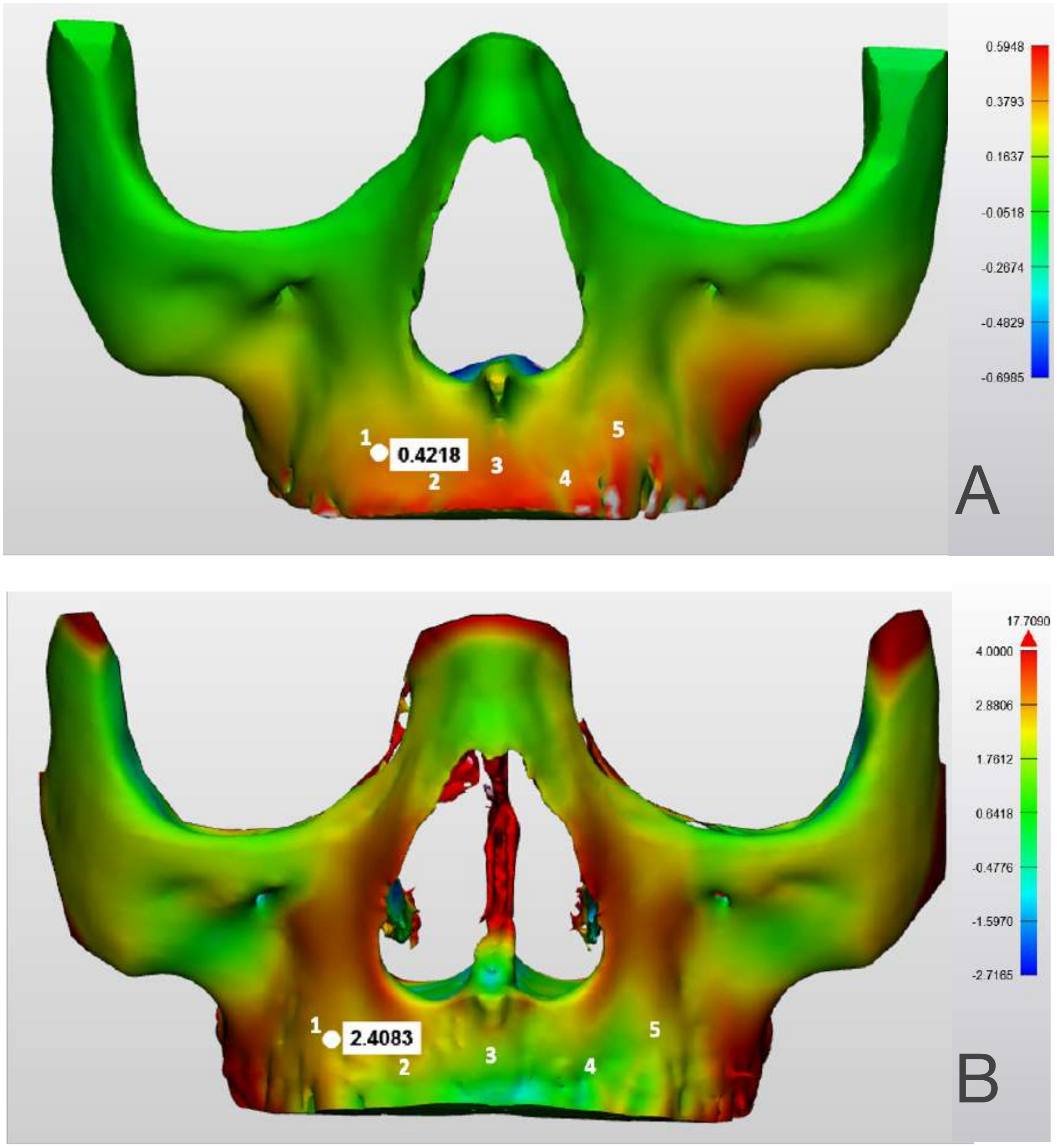


Figure 8.6: A illustrates the **modeled deformation (PCAmD)** through a color-coded map based on simulations. **B** illustrates the **actual deformation (PCAaD)** measured from an actual patient (FM-patient). Each color-coded map represents varying degrees of displacement, with the corresponding displacement values indicated by the scale (in mm) depicted next to each visualization. The maps clearly illustrate differences between simulated (predicted) and actual measured deformation. Five points are marked on each model for quantitative comparison between the simulation and the real-world results (numbers depicted in white 1 – 5). Detailed color-coded maps for each patient are available in figure 6.10.

RESULTS

Stress-distribution

Maxillary stress distribution (Figure 8.7)

Both the FM and MP treatment groups exhibited high local stress just below the zygomatic bone, specifically in the area apical to the first molar, where the applied forces are transferred to the bone. The magnitude of the stresses varied among patients, corresponding to the thickness of the cortical bone. Thinner bone in this region correlated with greater stress distribution. Maxillary stress distribution varied from 0.001 Mpa to 5 Mpa, with all MP models exhibiting a small region of very high stress below the zygomatic bone, precisely where the elastic forces originated. This difference in stress distribution was treatment-specific rather than patient-specific. It is likely attributable to the slightly more medial and less downward vector of the forces in the MP group (averaging 25 degrees) compared to the FM group (averaging 30 degrees downward). These subtle differences in force direction highlight the impact of treatment mechanics on stress distribution within the craniofacial structures.

Mandibular stress distribution (Figure 8.7)

The scales in figure 6.7 indicate that stresses in the mandible are ten times smaller than those in the maxilla, ranging from 0.0001 Mpa to 0.7 Mpa. This difference is attributed to the mandible's thicker cortical bone, which has a higher Young's modulus. The primary stress regions in the mandible are located in the symphyseal area. Additionally, the stress distribution patterns in the mandible differ between the two treatment options. In the FM group, stress in the symphyseal region is more evenly distributed along the entire mandible. In contrast, the MP group exhibits higher and more localized stresses concentrated around the area where the MP is attached to the bone. Interestingly, one patient-specific model showed unilaterally higher stress distribution in both the upper and lower jaws. This finding could only be attributed to individual patient-specific characteristics.

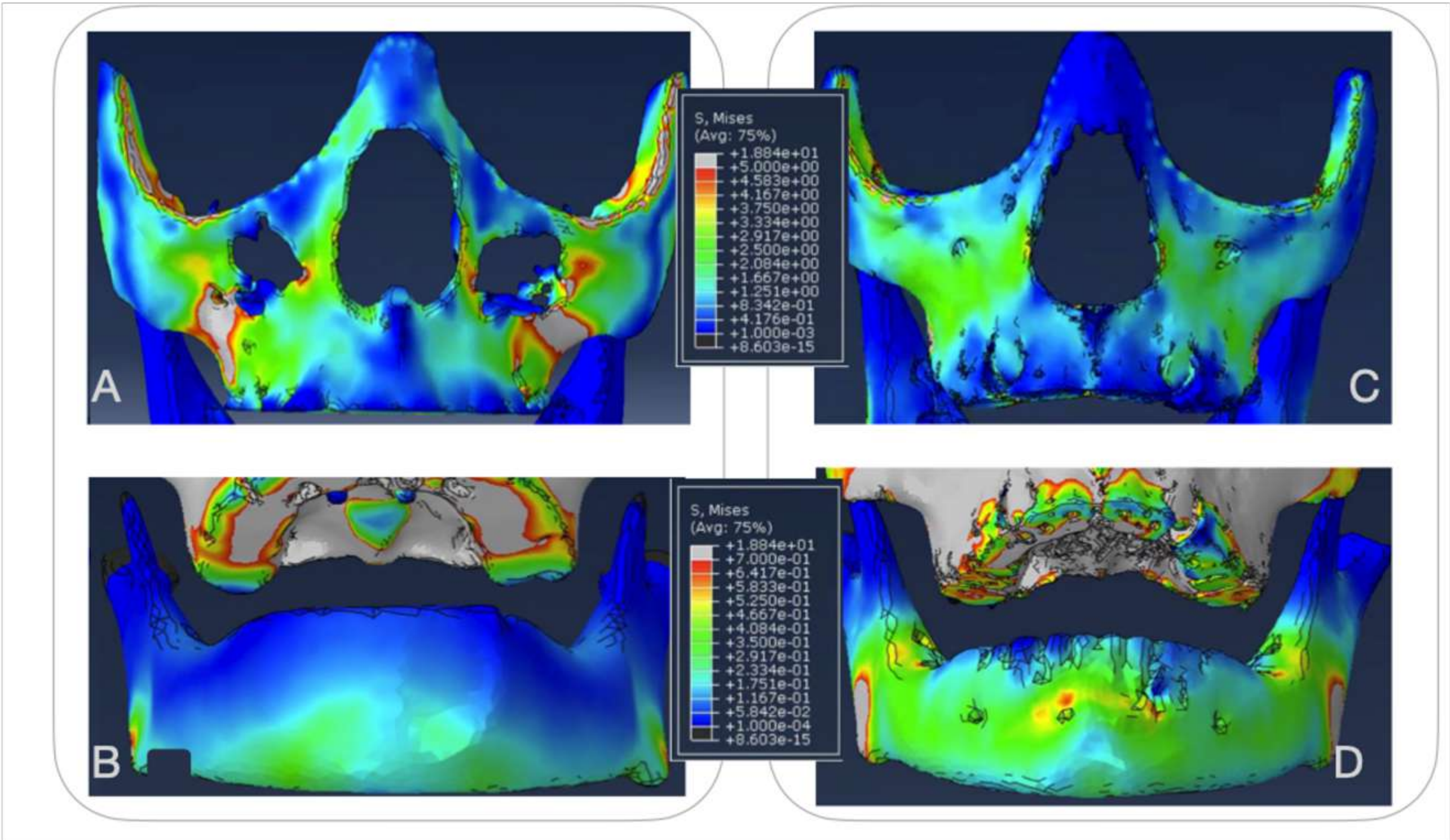


Figure 8.7: **Images A and C (upper jaw)** show stress distribution ranging from 0.001 MPa (dark blue, indicating minimal stress) to 5 MPa (bright red, indicating maximal stress). **Images B and D (lower jaw)** illustrate stress distribution ranging from 0.0001 MPa (dark blue, minimal stress) to 0.7 MPa (bright red, maximal stress).

Modelled deformation (PCAmD)

Looking at the overall deformation, maxillary deformation patterns revealed a patient-specific response (Figure 8.8), with less deformation observed in patients with thicker cortical bone, regardless of the treatment type. Although stress patterns differed between the FM and MP groups, these differences did not influence maxillary deformation. In contrast, mandibular deformation exhibited clear treatment-specific patterns, with the MP group showing greater deformation than the FM group. The model deformation was analyzed both overall and along three coordinate axes: transverse (x), sagittal (y), and vertical (z). On the x-axis, positive values indicate leftward movement, negative values rightward movement. On the y-axis, positive values represent backward movement, negative values forward movement. On the z-axis, positive values show upward movement, negative values downward movement. The results display displacement patterns using a color-coded system, with red indicating maximum displacement and blue showing minimum displacement. Figures 6.8 illustrate the displacement patterns for all four patients across three axes. In the x-axis, maximum deformation occurs in the posterior maxillary region apical of the first and second molars. These deformations ranged from 0.27 mm to the left to 2.74 mm to the right and were patient-specific. The midface shows minimal deformation, and the mandible remains largely stable except for minor condylar changes. Treatment-specific effects are evident in both jaws in the y-axis: Facemask patients show greater upper jaw deformation and mentoplate patients display greater lower jaw deformation. Mentoplate patients showed more anterior mandibular movement than facemask patients. This movement likely results from counterclockwise mandibular rotation around the mandibular angle, explaining backward condylar displacement. The z-axis analysis confirms these treatment-specific vertical differences in the mandible. Interestingly, deformation in the upper jaw also showed counterclockwise rotation due inferior displacement of the posterior part of the palate, which was not treatment specific (downward displacement ranged from 0.57 to 1.2 mm).

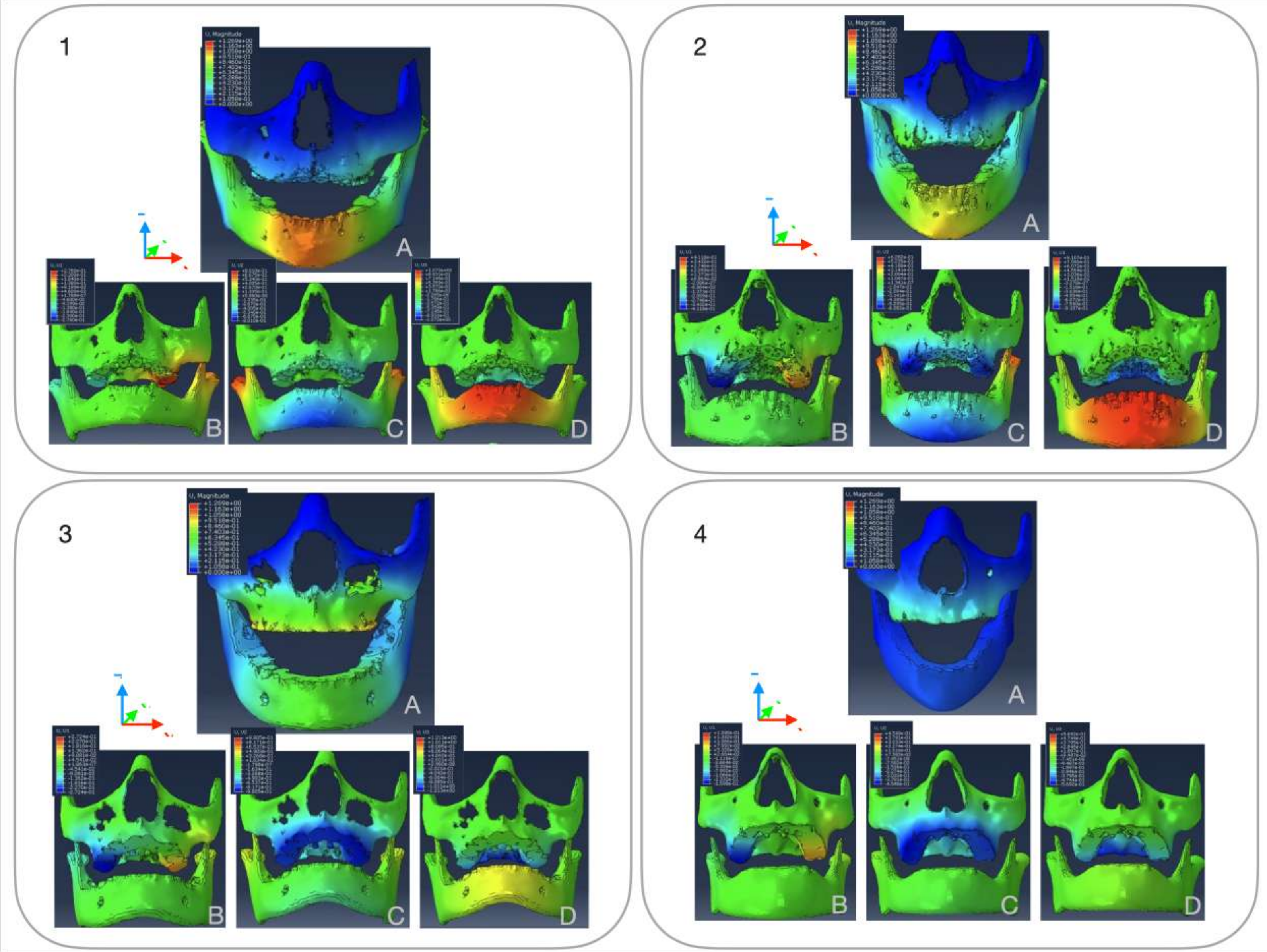


Figure 8.8: Three-dimensional FEM of upper and lower jaw frontal view of 4 patients. Color-coded displacement patterns are displayed in (A)overall displacement pattern and along three coordinate axes: B. x-axis (lateral), C. y-axis (sagittal) and D. z-axis (vertical). Patient 1 and 2 used mentoplate, patients 3 and 4 used facemask. Each color-coded map represents varying degrees of displacement, with the corresponding displacement values indicated by the scale (in mm) depicted next to each visualization.

Comparing modeled deformation (PCAmD) with actual deformation (PCAaD)

The modeled values (PCAmD) were found to be ten times smaller than the actual one-year deformation analysis (PCAaD) (Figures 8.9 and 8.10). A patient-by-patient comparison revealed discrepancies and similarities. Cases with the highest predicted deformation occasionally exhibited lower actual changes, while cases with similar predicted patterns showed widely varying clinical outcomes. Notably, no consistent relationship could be identified between the model predictions and treatment success in the upper jaw (Figure 8.10). Quantitative analysis of 6 additional upper jaws, using five anatomical landmarks per patient, revealed no correlation between PCAmD and PCAaD measurements. PCAmD values ranged from 0.11 to 0.51 mm (mean: 0.35 ± 0.12 mm), while PCAaD values ranged from 0.43 to 3.12 mm (mean: 1.61 ± 0.64 mm) (Table 8.1).

Table 8.1: measurements (mm) of changes at 5 anatomical points

	point 1		point 2		point 3		point 4		point 5	
	PCAmD	PCAaD	PCAmD	PCAaD	PCAmD	PCAaD	PCAmD	PCAaD	PCAmD	PCAaD
MP 1	0,22	1,75	0,33	1,50	0,35	1,57	0,51	1,03	0,49	1,90
MP 2	0,22	0,43	0,30	1,42	0,38	1,16	0,46	0,71	0,34	0,59
MP3	0,11	3,12	0,15	2,42	0,15	2,73	0,16	2,08	0,18	2,84
FM 1	0,42	2,41	0,43	2,33	0,48	0,75	0,43	0,69	0,41	1,78
FM2	0,39	0,90	0,49	1,66	0,46	1,79	0,48	1,55	0,38	1,28
FM 3	0,30	2,21	0,35	1,85	0,43	1,10	0,34	1,48	0,43	1,37

PCAmD: modelled deformation; PCAaD: actual treatment effect after 1 year (PCAaD); FM: facemask; MP: mentoplate.

Matching mandibular deformation with actual treatment effect proved more complex than analyzing those of the maxilla due to the lack of a fixed point of reference on the mandible. Additionally, the observed mandibular changes were consistently smaller than the finite element analysis (FEA) predictions, suggesting that our reference of boundary condition obscured critical details. As a result, comparing modeled deformation with actual deformation for the mandible was not feasible within the limitations of the current FE model (Figure 8.9).

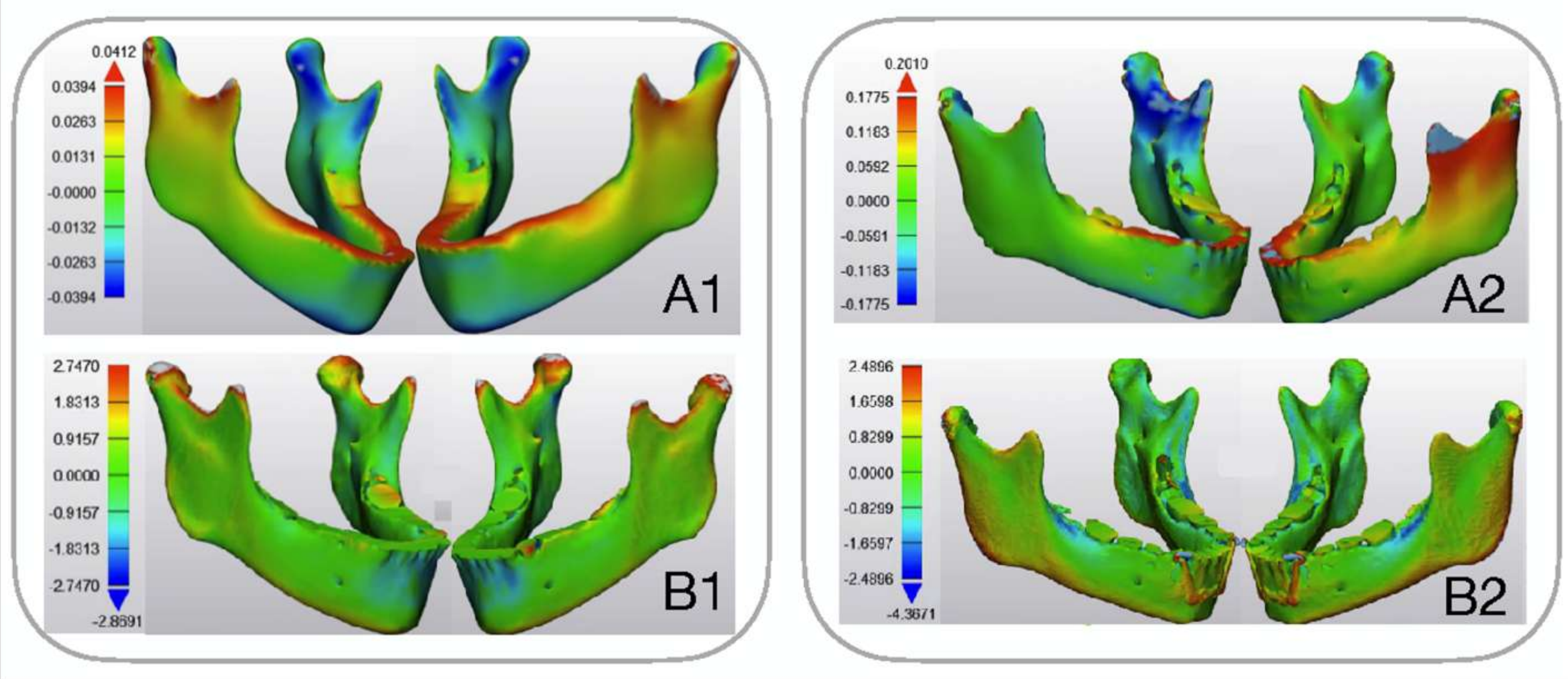


Figure 8.9: A. Three-dimensional FEM showing displacement in color coded map of modelled deformation (PCAmD) and B. color coded map of actual deformation (PCAaD). Patient 1 received facemask treatment and patient 2 received mentoplate treatment. Each color-coded map represents varying degrees of displacement, with the corresponding displacement values indicated by the scale (in mm) depicted next to each visualization.

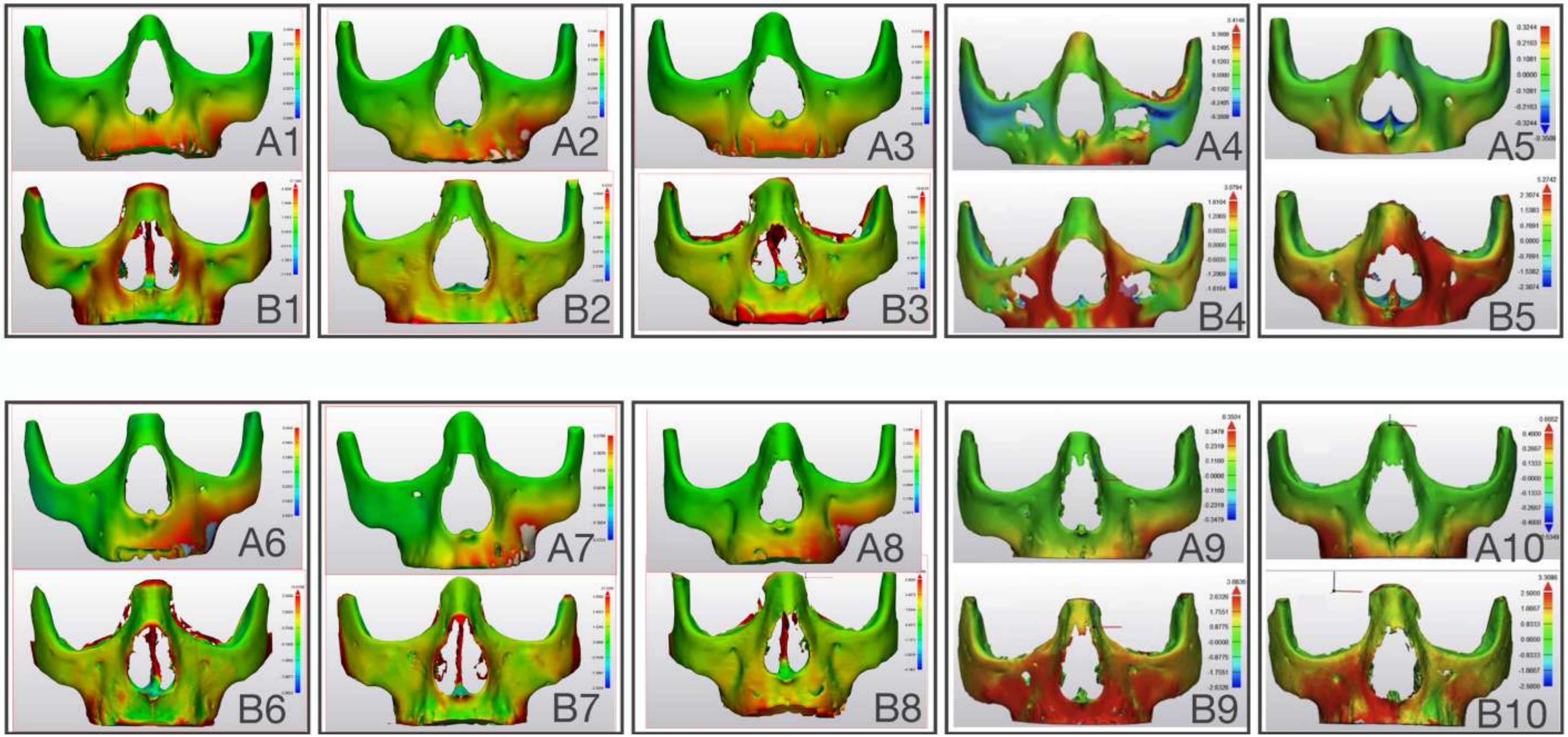


Figure 8.10: A. Three-dimensional FEM showing displacement in color coded map of modelled deformation (PCAmD) and B. color coded map of actual deformation (PCAaD). Patients 1- 5 received facemask treatment and patients 6 - 10 received mentoplate treatment. Each color-coded map represents varying degrees of displacement, with the corresponding displacement values indicated by the scale (in mm) depicted next to each visualization.

DISCUSSION

Class III interceptive treatment is difficult and often leaves clinicians with questionable or poor results in terms of occlusion or facial esthetics, even when the initial treatment effect appears good [4]. Over time, as the patient fully matures, relapse can occur, leading to an end result that is less than ideal. Limited research exists on the long-term outcomes of early Class III malocclusion treatment, but approximately 25 – 30 % could benefit from orthognathic surgery after interceptive maxillary protraction therapy [44,45] . Identifying patients likely to benefit from interceptive treatment with minimal risk of relapse is critical. For those unlikely to respond well, delaying treatment until growth completion followed by orthognathic surgery may be a more effective strategy. Predictive factors for treatment success are often derived from 2D cephalometric analyses or linear/angular measurements from cone-beam computed tomography (CBCT) scans [14–16]. Emerging models now integrate these measurements with the initial treatment response to optimize decision-making and reduce the likelihood of unsuccessful outcomes [17]. However, most of this research is retrospective and lacks proper validation on new cases, making their predictive accuracy uncertain [14]. Our approach expanding this research in a 3-dimensional approach, tries to investigate whether a patient specific FEM could serve as a potential predictive tool. While FEM is commonly used to study tooth movement in orthodontics [46], few studies have validated their predictions against actual clinical outcomes [47,48]. Current FEM research on maxillary protraction therapy typically uses idealized models rather than patient-specific data, and lacks clinical validation [25,28,49]. A lot of variability can be observed in FEM exploring the effect of maxillary protraction therapy, with varying degree of detailing visualizing bone, sutures, periodontal ligament and teeth. Most assume isotropic homogeneous properties, despite evidence suggesting more complex characteristics, especially in the upper jaw [50]. This simplification may affect model accuracy at the individual patient level. Although some previous studies have attempted to model both jaws simultaneously [28], they typically lack detailed TMJ representation and some rely on adult dry skull specimens rather than age-appropriate samples [26]. Our simplified FEM deformation largely aligns with previous studies on maxillary protraction using skeletal anchorage devices [26–28,49]. Despite using different boundary conditions for the upper and lower jaw, we observed similar deformation patterns, specifically a counterclockwise (CCW) rotation of the craniomaxillary complex. The maxilla moves forward with downward displacement of the posterior palate, causing CCW rotation of the upper jaw [26–28]. Our mentoplate FEM shows CCW rotation of the lower jaw with anterior displacement of the mandibular symphysis, consistent with previous research using symphyseal plates [28]. However, the literature shows some contradictions. Some studies report less deformation with skeletal anchorage (SA) devices compared to tooth-borne (TB) solutions [27], while others show similar results [26]. Palatal anchorage devices may produce greater deformation [26]. Studies also differ on rotational effects, with some showing less CCW rotation in SA versus TB [27], while others indicate similar vertical control [26]. Given these inconsistencies, we should be cautious about drawing clinical conclusions from these studies. Additionally, no research has yet compared FEM predictions with actual treatment outcomes in maxillary protraction therapy.

This study is the first to directly compare biomechanical model predictions with clinical outcomes in maxillary protraction therapy. Our findings reveal no correlation between predicted and actual treatment effects, with clinical results approximately 10 times greater than model predictions Figures 8.9 and 8.10 illustrate these comparisons, with color-coded visualizations highlighting differences in deformation magnitudes and directions. The analysis revealed areas of alignment as well as discrepancies, shedding light on both the strengths and limitations of the FE modeling approach. This discrepancy suggests that current FEM approaches for maxillary protraction therapy, while valuable for understanding force distribution, may be insufficient for clinical decision-making in growing patients. While the upper jaw deformation patterns aligned with previous studies, the model's simplicity omitted crucial elements such as sutures, teeth, and periodontal ligaments. The lower jaw model proved particularly unreliable mainly due to oversimplified boundary conditions at the mandibular angle. This discrepancy highlights significant model limitations: 1. Oversimplified anatomy (omitting sutures, teeth, and periodontal ligaments) 2. Separate analysis of upper and lower jaws, ignoring their interconnected nature and the documented remodeling of the mandibular condyle and glenoid fossa during treatment [51] 3. Assumption of homogeneous bone properties 4. Exclusion of biological processes (growth, bone remodeling and post-treatment relapse) 5. Omission of muscular, masticatory, and soft tissue effects. These limitations suggest the need for more sophisticated models incorporating patient-specific data and biological processes. Another limitation of this study was the absence of mesh convergence testing, which is essential to validate the numerical stability and accuracy of finite element models. The selected mesh sizes were based on prior studies and anatomical considerations; however, future research should include systematic convergence testing to ensure that the results are independent of mesh density. Such testing will enhance the reliability of finite element models for clinical applications. While applying forces directly to nodes simplifies the modeling process, the authors recognize that selecting a surface, coupling it to a reference point, and applying the force to the reference point is an alternative approach that can more accurately distribute forces over a region. Future studies may explore this method to further refine loading conditions and improve the biomechanical representation of force applications in FEMs.

The study reveals that patient characteristics, particularly bone thickness, had a greater impact on deformation patterns than the type of treatment used. FM and MP treatments showed similar effects, indicating treatment choice does not significantly influence deformation patterns. Modeling the mandible accurately is difficult due to its complex structure and the temporomandibular joint (TMJ) mechanics. While the mandibular angle seems ideal for setting boundary conditions, applying constraints here can create artificial forces. To address this, developing a detailed TMJ model in Abaqus® could better simulate mandibular movement. Although our simplified finite element model (FEM) showed deformation patterns consistent with previous studies on maxillary protraction therapy, it could not accurately predict treatment outcomes. Ultimately, patient-specific factors, not treatment type, were most influential in deformation pattern.

Although this proof-of-concept study involved a small sample size, the consistent discrepancy between model predictions and clinical results underscores the reliability of the findings. Future research should expand to include a larger patient cohort and consider additional factors beyond anatomical properties. Furthermore, integrating advanced methodologies such as radiomics, genomics, and biological markers could pave the way for more precise and individualized treatment predictions.

CONCLUSION

Our systematic analysis highlighted fundamental limitations in current modeling approaches for maxillary protraction therapy, particularly those relying solely on anatomical models. Although our simplified FEM had substantial limitations, deformation pattern aligned with previously reported maxilary protraction therapy models. These findings underscore the inadequacy of purely biomechanical simulations to capture the complexity of craniofacial treatment dynamics. Importantly, the analysis revealed that patient-specific characteristics, rather than treatment type, play a dominant role in determining deformation patterns. This suggests that successful predictive tools must integrate a broader range of factors beyond biomechanics alone.

Future predictive models should incorporate a combination of biological markers, growth patterns, and patient-specific tissue responses to more accurately reflect the multifaceted nature of craniofacial adaptation. Such advancements will likely require the use of artificial intelligence (AI) and machine learning to process and analyze the vast amount of data needed to capture these interactions. Until these sophisticated, integrated models are developed and validated, clinicians should exercise caution when relying on biomechanical models for treatment planning in maxillary protraction therapy. Instead, these tools should be regarded as supplementary aids rather than definitive predictors of treatment success.

Ethical approval

This RCT was registered at www.clinicaltrials.gov (ID: NCT02711111) and ethical approval was granted by the by the Ethics Committee at the Ziekenhuis Oost Limburg, Belgium (EudraCT B371201629565) (13/12/2016).

REFERENCES

1. Woon, See Choong, and Badri Thiruvenkatachari. 2017. Early orthodontic treatment for Class III malocclusion: A systematic review and meta-analysis. *American journal of orthodontics and dentofacial orthopedics : official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics* 151: 28–52. https://doi.org/10.1016/j.ajodo.2016.07.017.
2. De Toffol, Laura, Chiara Pavoni, Tiziano Baccetti, Lorenzo Franchi, and Paola Cozza. 2008. Orthopedic Treatment Outcomes in Class III Malocclusion. *Angle Orthodontist* 78. https://doi.org/10.2319/030207-108.1.
3. Rongo, Roberto, Vincenzo D'Antò, Rosaria Bucci, Ilaria Polito, Roberto Martina, and Ambrosina Michelotti. 2017. Skeletal and dental effects of Class III orthopaedic treatment: a systematic review and meta-analysis. *Journal of oral rehabilitation*. https://doi.org/10.1111/joor.12495.
4. Mandall, Nicky, Richard Cousley, Andrew Dibiase, Fiona Dyer, Simon Littlewood, Rye Mattick, Spencer J Nute, et al. 2016. Early class III protraction facemask treatment reduces the need for orthognathic surgery: a multi-centre, two-arm parallel randomized, controlled trial. *Journal of Orthodontics* 43. Taylor & Francis: 164–175. https://doi.org/10.1080/14653125.2016.1201302.
5. Ngan, P. W., U. Hagg, C. Yiu, and S. H. Wei. 1997. Treatment response and long-term dentofacial adaptations to maxillary expansion and protraction. *Seminars in orthodontics* 3: 255–264. https://doi.org/10.1016/S1073-8746(97)80058-8.
6. Hu, Shoushan, Ke An, and Yiran Peng. 2022. Comparative efficacy of the bone-anchored maxillary protraction protocols for orthopaedic treatment in skeletal Class III malocclusion: A Bayesian network meta-analysis. *Orthodontics and Craniofacial Research* 25: 243–250. https://doi.org/10.1111/ocr.12532.
7. YILDIRIM, Gamze, Elvan ONEM OZBİLEN, and Fulya ÖZDEMİR. 2023. Retrospective 3-dimensional Evaluation of Skeletal and Dental Structures Following Treatment with Hybrid Hyrax-Mentonplate with Class III Elastics in Class III Patients with Vertical Growth Pattern: A Pilot Study. *European Journal of Research in Dentistry* Cilt:7 Say: 78–87. https://doi.org/10.29228/erd.49.
8. Willmann, Jan H., Manuel Nienkemper, Nour Eldin Tarraf, Benedict Wilmes, and Dieter Drescher. 2018. Early Class III treatment with Hybrid-Hyrax – Facemask in comparison to Hybrid-Hyrax-Mentoplate – skeletal and dental outcomes. *Progress in Orthodontics* 19. Progress in Orthodontics: 0–7. https://doi.org/10.1186/s40510-018-0239-8.
9. Ergul, Tugce, and Aysegul Gulec. 2024. Comparison of the effectiveness of skeletal and tooth-borne protraction methods with or without alternate rapid maxillary expansion and constriction protocol in patients with Class III malocclusion. *American Journal of Orthodontics and Dentofacial Orthopedics* article in. American Association of Orthodontists. https://doi.org/10.1016/j.ajodo.2024.10.010.
10. Mandall, Nicky, Wesam Aleid, Richard Cousley, Edith Curran, Susi Caldwell, Andrew DiBiase, Fiona Dyer, et al. 2024. The effectiveness of bone anchored maxillary protraction (BAMP) in the management of class III skeletal malocclusion in children aged 11–14 years compared with an untreated control group: A multicentre two-arm parallel randomised controlled trial. *Journal of Orthodontics*. https://doi.org/10.1177/14653125241255139.

11. Cornelis, Marie A., Michele Tepedino, Neel De Vos Riis, Xiaowen Niu, and Paolo M. Cattaneo. 2021. Treatment effect of bone-Anchored maxillary protraction in growing patients compared to controls: A systematic review with meta-Analysis. *European Journal of Orthodontics* 43: 51–68. https://doi.org/10.1093/ejo/cjaa016.
12. Meyns, J., D. M. Brasil, J. F. Mazzi-Chaves, C. Politis, and R. Jacobs. 2018. The clinical outcome of skeletal anchorage in interceptive treatment (in growing patients) for class III malocclusion. *International Journal of Oral and Maxillofacial Surgery* 47. International Association of Oral and Maxillofacial Surgery: 1003–1010. https://doi.org/10.1016/j.ijom.2018.04.011.
13. Kinzinger, Gero Stefan Michael, Jan Hourfar, Joana Nanina Sommer, and Jörg Alexander Lisson. 2024. Age-dependent effects of Delaire facemask therapy for class III malocclusion: Impact on maxillary sutures and palatal morphology. *Journal of Orofacial Orthopedics*. https://doi.org/10.1007/s00056-024-00564-9.
14. Fudalej, Piotr, Magdalena Dragan, and Barbara Wedrychowska-Szulc. 2011. Prediction of the outcome of orthodontic treatment of Class III malocclusions-a systematic review. *European Journal of Orthodontics* 33: 190–197. https://doi.org/10.1093/ejo/cjq052.
15. Lee, Mi So, Van Nhat Thang Le, Jae Gon Kim, Yeon Mi Yang, and Dae Woo Lee. 2023. Prediction Model for Future Success of Early Orthopedic Treatment of Class III Malocclusion. *Children* 10: 1–11. https://doi.org/10.3390/children10020355.
16. Choi, Yoon Jeong, Jeong Eun Chang, Chooryung J. Chung, Ji Hyun Tahk, and Kyung Ho Kim. 2017. Prediction of long-term success of orthopedic treatment in skeletal Class III malocclusions. *American Journal of Orthodontics and Dentofacial Orthopedics* 152. American Association of Orthodontists: 193–203. https://doi.org/10.1016/j.ajodo.2016.12.018.
17. Kong, Hong, Peter Ngan, DABPedD Stephen Hon-Yin Wei, and Professor Stephen Hon-Yin Wei. 2004. Early Treatment of Class III Patients To Improve Facial Aesthetics and Predict Future Growth. *Dental Journal* 1: 24–30.
18. Miki, M. 1979. [An experimental research on the directional control of the nasomaxillary complex by means of external force--two dimensional analysis on the sagittal plane of the craniofacial skeleton (author’s transl)]. *Shika gakuho. Dental science reports* 79. Japan: 1563–1597.
19. Hirato, R. 1984. [An experimental study on the center of resistance of the nasomaxillary complex. 2-dimensional analysis of the coronal plane in the dry skull]. *Shika gakuho. Dental science reports* 84. Japan: 1225–1262.
20. Lee, K. G., Y. K. Ryu, Y. C. Park, and D. J. Rudolph. 1997. A study of holographic interferometry on the initial reaction of maxillofacial complex during protraction. *American journal of orthodontics and dentofacial orthopedics : official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics* 111: 623–632. https://doi.org/10.1016/S0889-5406(97)70314-7.
21. Nanda, R. 1978. Protraction of maxilla in rhesus monkeys by controlled extraoral forces. *American journal of orthodontics* 74. United States: 121–141. https://doi.org/10.1016/0002-9416(78)90080-5.
22. Billiet, Toon, Guy De Pauw, and Luc Dermaut. 2001. Location of the centre of resistance of the upper dentition and the nasomaxillary complex. An experimental study. *European Journal of Orthodontics* 23: 263–273. https://doi.org/10.1093/ejo/23.3.263.
23. Itoh, T, S J Chaconas, A A Caputo, and J Matyas. 1985. Photoelastic effects of maxillary protraction on the craniofacial complex. *American journal of orthodontics* 88. United States: 117–124. https://doi.org/10.1016/0002-9416(85)90235-0.

24. Caputo, Angelo A., Spiro J. Chaconas, and Riley K. Hayashi. 1974. Photoelastic visualization of orthodontic forces during canine retraction. *American Journal of Orthodontics* 65: 250–259. https://doi.org/10.1016/S0002-9416(74)90330-3.
25. Suresh, Sugitha, Shobha Sundareswaran, and Sreehari Sathyanadhan. 2021. Effect of microimplant assisted rapid palatal expansion on bone-anchored maxillary protraction: A finite element analysis. *American Journal of Orthodontics and Dentofacial Orthopedics* 160. American Association of Orthodontists: 523–532. https://doi.org/10.1016/j.ajodo.2020.04.040.
26. Kim, Kwang Yoo, Mohamed Bayome, Jae Hyun Park, Ki Beom Kim, Sung Seo Mo, and Yoon Ah Kook. 2015. Displacement and stress distribution of the maxillofacial complex during maxillary protraction with buccal versus palatal plates: Finite element analysis. *European Journal of Orthodontics* 37: 275–283. https://doi.org/10.1093/ejo/cju039.
27. Yan, Xiulin, Weijun He, Tao Lin, Jun Liu, Xiaofeng Bai, Guangqi Yan, and Li Lu. 2013. Three-dimensional finite element analysis of the craniomaxillary complex during maxillary protraction with bone anchorage vs conventional dental anchorage. *American Journal of Orthodontics and Dentofacial Orthopedics* 143: 197–205. https://doi.org/10.1016/j.ajodo.2012.09.019.
28. Shyagali, Tarulatha R., Rahul Patidar, Abhishek Gupta, Shanya Kapoor, and Anil Tiwari. 2023. Evaluation of stresses and displacement in the craniofacial region as a reaction to bone-anchored maxillary protraction in conjugation with posterior bite plane and rapid maxillary expansion in patients with Class III malocclusion: A finite element analys. *American Journal of Orthodontics and Dentofacial Orthopedics* 164. American Association of Orthodontists: 253–264. https://doi.org/10.1016/j.ajodo.2022.12.015.
29. Balakrishnan, Rajkumar, Nagalakshmi Sengottuvel, Syed Khalid Altaf, Pawan Kumar Bhandari, Preethi Kumaragurubaran, and Marshal Antony. 2023. Three-Dimensional Finite Element Analysis of Maxillary Protraction Using Diverse Modes of Rapid Palatal Expansion. *Cureus* 15. https://doi.org/10.7759/cureus.36328.
30. Liou, Eric Jein Wein, and Wen Ching Tsai. 2005. A new protocol for maxillary protraction in cleft patients: Repetitive weekly protocol of alternate rapid maxillary expansions and constrictions. *Cleft Palate-Craniofacial Journal* 42: 121–127. https://doi.org/10.1597/03-107.1.
31. Wood, Sarah A, David S Strait, Elizabeth R Dumont, Callum F Ross, and Ian R Grosse. 2011. The effects of modeling simplifications on craniofacial finite element models: the alveoli (tooth sockets) and periodontal ligaments. *Journal of biomechanics* 44. United States: 1831–1838. https://doi.org/10.1016/j.jbiomech.2011.03.022.
32. Lee, B., C. Flores-Mir, and M. O. Lagravère. 2016. Normal orbit skeletal changes in adolescents as determined through cone-beam computed tomography. *Head and Face Medicine* 12. Head & Face Medicine: 10–15. https://doi.org/10.1186/s13005-016-0130-0.
33. Nguyen, Tung, Lucia Cevidanes, Lorenzo Franchi, Antonio Ruellas, and Tate Jackson. 2018. Three-dimensional mandibular regional superimposition in growing patients. *American Journal of Orthodontics and Dentofacial Orthopedics* 153. American Association of Orthodontists: 747–754. https://doi.org/10.1016/j.ajodo.2017.07.026.
34. LeCornu, Megan, Lucia Helena Soares Cevidanes, Zhu Hongtu, Chih-Da Wu, Brent Larson, and Tung T. Nguyen. 2013. Three-dimensional treatment outcomes in class II patientes treated with Herbst appliance: A pilot study. *Am J orthod*

Dentofacial orthop 144: 1-818–830. https://doi.org/10.1016/j.ajodo.2013.07.014.Three-dimensional.

35. Ngan, Peter, Benedict Wilmes, Dieter Drescher, Chris Martin, Bryan Weaver, and Erdogan Gunel. 2015. Comparison of two maxillary protraction protocols: tooth-borne versus bone-anchored protraction facemask treatment. *Progress in orthodontics* 16: 26. https://doi.org/10.1186/s40510-015-0096-7.
36. Wilmes, Benedict, Manuel Nienkemper, Björn Ludwig, Chung How Kau, and Dieter Drescher. 2011. Early Class III treatment with a hybrid hyrax-mentoplate combination. *Journal of clinical orthodontics: JCO*: 15–21.
37. Kim, J H, M a Viana, T M Graber, F F Omerza, and E a BeGole. 1999. The effectiveness of protraction face mask therapy: a meta-analysis. *American journal of orthodontics and dentofacial orthopedics : official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics* 115: 675–685. https://doi.org/10.1016/S0889-5406(99)70294-5.
38. Gazzani, Francesca, Chiara Pavoni, Aldo Giancotti, Paola Cozza, and Roberta Lione. 2018. Facemask performance during maxillary protraction: a finite element analysis (FEA) evaluation of load and stress distribution on Delaire facemask. *Progress in Orthodontics* 19. Progress in Orthodontics: 1–5. https://doi.org/10.1186/s40510-018-0217-1.
39. Anirudh Agarwal, Rinku Mathur. 2010. Maxillary Expansion. *International Journal of Clinical Pediatric Dentistry* 3: 139–146.
40. Goeckner, Kelly, Venkatram Pepakayala, Jeanne Nervina, Yogesh Gianchandani, and Sunil Kapila. 2016. Three-dimensional force measurements during rapid palatal expansion in Sus scrofa. *Micromachines* 7: 1–11. https://doi.org/10.3390/mi7040064.
41. Isaacson, R.J., J.L. Wood, and A.H. Ingram. 1964. Forces produced by rapid maxillary expansion: II. Forces present during treatment. *Angle Orthodontist* 34: 261–278.
42. Pluim, Josien P.W., J. B.A.Antoine Maintz, and Max A. Viergever. 2003. Mutual-information-based registration of medical images: A survey. *IEEE Transactions on Medical Imaging* 22: 986–1004. https://doi.org/10.1109/TMI.2003.815867.
43. Maes, Frederik, Andre Collignon, Dirk Vandermeulen, Guy Marchal, and Paul Suetens. 1996. Multi-modality image registration by maximization of mutual information. *Proceedings of the Workshop on Mathematical Methods in Biomedical Image Analysis* 16: 14–22. https://doi.org/10.1109/mmbia.1996.534053.
44. Owens, D., Simon Watkinson, Jayne E. Harrison, S. Turner, and Helen V. Worthington. 2024. Orthodontic treatment for prominent lower front teeth (Class III malocclusion) in children (Review). *Cochrane Database of Systematic Reviews* 2024. https://doi.org/10.1002/14651858.CD003451.pub2.
45. Lin, Yifan, Runzhi Guo, Liyu Hou, Zhen Fu, and Weiran Li. 2018. Stability of maxillary protraction therapy in children with Class III malocclusion: a systematic review and meta-analysis. *Clinical Oral Investigations* 22. Clinical Oral Investigations: 2639–2652. https://doi.org/10.1007/s00784-018-2363-8.
46. Knop, Luegya, Luiz Gonzaga Gandini, Ricardo Lima Shintcovsk, and Marcia Regina Elisa Aparecida Schiavon Gandini. 2015. Scientific use of the finite element method in orthodontics. *Dental Press Journal of Orthodontics* 20: 119–125. https://doi.org/10.1590/2176-9451.20.2.119-125.sar.
47. Likitmongkolsakul, Udomsak, Pruittikorn Smithmaitrie, Bancha Samruajbenjakun, and Juthatip Aksornmuang. 2018. Development and Validation of 3D Finite Element Models for Prediction of Orthodontic Tooth Movement. *International Journal of Dentistry* 2018.

https://doi.org/10.1155/2018/4927503.
48. Jiang, Jingang, Liang Yao, Yongde Zhang, Xuefeng Ma, Yafeng Guo, and Yi Liu. 2022. Establishment, FEM analysis and experimental validation of tooth movement prediction model of orthodontic archwire T-loop. *BMC Oral Health* 22. BioMed Central: 1–15. https://doi.org/10.1186/s12903-022-02430-9.
49. Rai, Priyank, Dhiraj Garg, Tulika Tripathi, Anup Kanase, and Gayatri Ganesh. 2021. Biomechanical effects of Skeletally anchored Class III elastics on the maxillofacial complex: a 3D finite element analysis. *Progress in Orthodontics* 22. Progress in Orthodontics. https://doi.org/10.1186/s40510-021-00375-3.
50. Peterson, Jill, Qian Wang, and Paul C. Dechow. 2006. Material properties of the dentate maxilla. *Anatomical Record - Part A Discoveries in Molecular, Cellular, and Evolutionary Biology* 288: 962–972. https://doi.org/10.1002/ar.a.20358.
51. De Clerck, Hugo, Tung Nguyen, Leonardo Koerich de Paula, and Lucia Cevidanes. 2012. Three-dimensional assessment of mandibular and glenoid fossa changes after bone-anchored Class III intermaxillary traction. *American journal of orthodontics and dentofacial orthopedics : official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics* 142: 25–31. https://doi.org/10.1016/j.ajodo.2012.01.017.

SUPPLEMENTARY MATERIALS

Node sets and force distribution per node

Forces were distributed throughout the bone rather than concentrated at a single point. To simulate this in the molar region, 20 nodes were selected on each side of the maxilla: 10 inside and 10 outside the dental arch. This dual-node placement creates realistic force dispersion. Each palatal screw is represented by 7 nodes surrounding the screw's segmentation in the model (Figure 6.11). Cross-sectional views revealed that node selection extends into the bone due to small holes created during the 1mm mesh construction. The chin-cup pressure is distributed across 43 nodes, matching the actual contact area. For mentoplate cases, each of the four screws is visualized and represented by six nodes (three outside and three inside the mandible) to simulate force dispersion in bone tissue. This method was chosen in an attempt to mimic realistic force distribution in the FEM, rather than creating a generalized model to compare both treatment techniques.

The total force was distributed across all nodes. The table below shows the per-node forces for each of the four patients, with forces varying along the x, y, and z axes due to patient-specific force vector designs. $F_{elastic}$ represents the force applied to the maxilla (upper jaw)

Component	$F_{elastic}$/node	$F_{expansion}$/node	F_{chin}/node
x	0	+/-0.908	0
y	-0.143	0	0.0667
x	-0.133	0	0.0622

Facemask patient 1overview of forces

Component	$F_{elastic}$/node	$F_{expansion}$/node	F_{chin}/node
x	0	+/-0.908	0
y	-0.141	0	0.071
x	-0.136	0	0.068

Facemask patient 2: overview of forces

Component	$F_{elastic}$/node	$F_{expansion}$/node	F_{chin}/node
x	+/-0.03	+/-0.923	0
y	-0.0724	0	0.1207
x	-0.0589	0	0.0982

Mentoplate patient 1: overview of forces

Component	$F_{elastic}$/node	$F_{expansion}$/node	F_{chin}/node
x	+/-0.043	+/-0.923	0
y	-0.0573	0	0.0955
x	-0.067	0	0.1117

Mentoplate patient 2: overview of forces

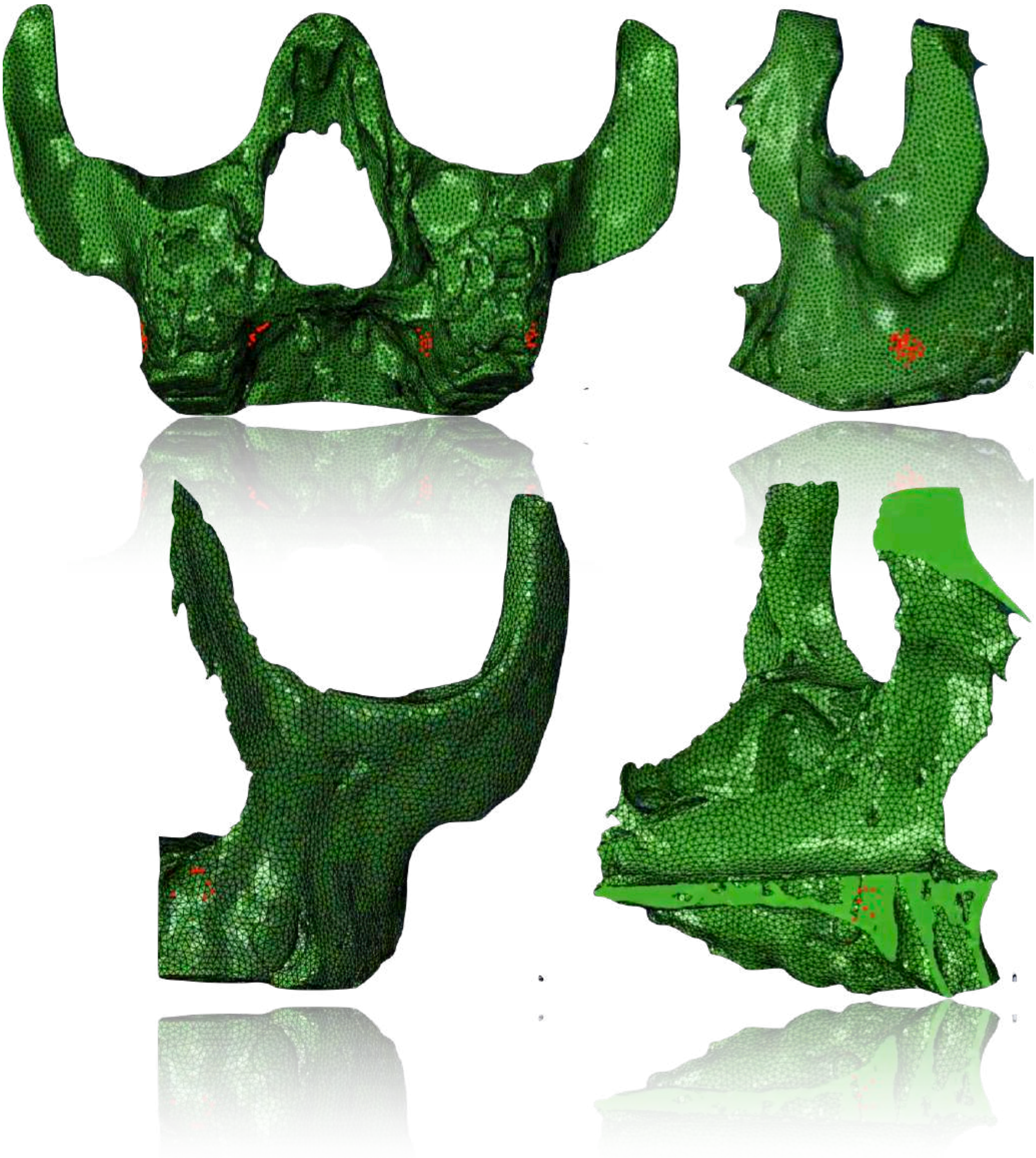


Figure 8.11: Detail of node position in the upper jaw

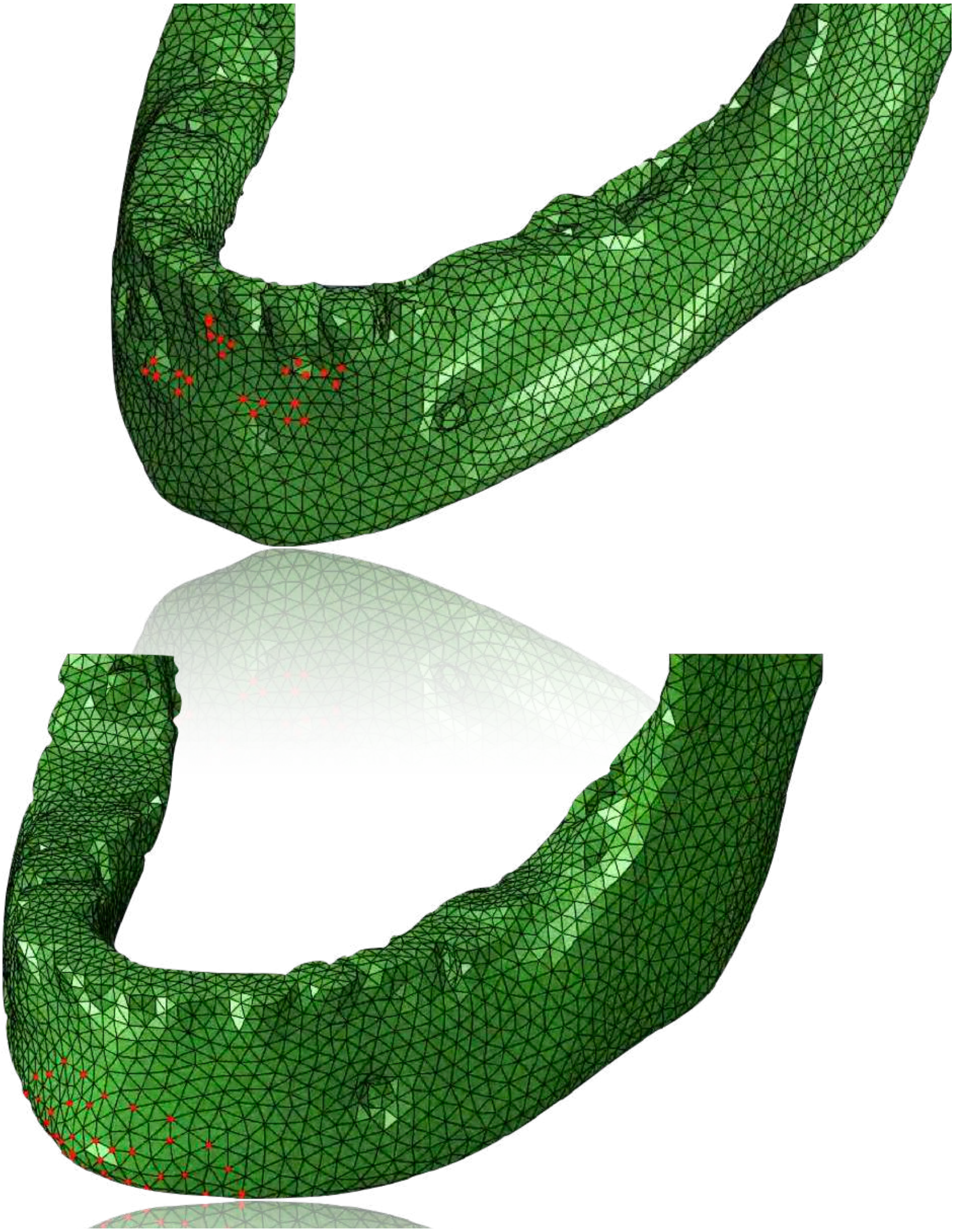
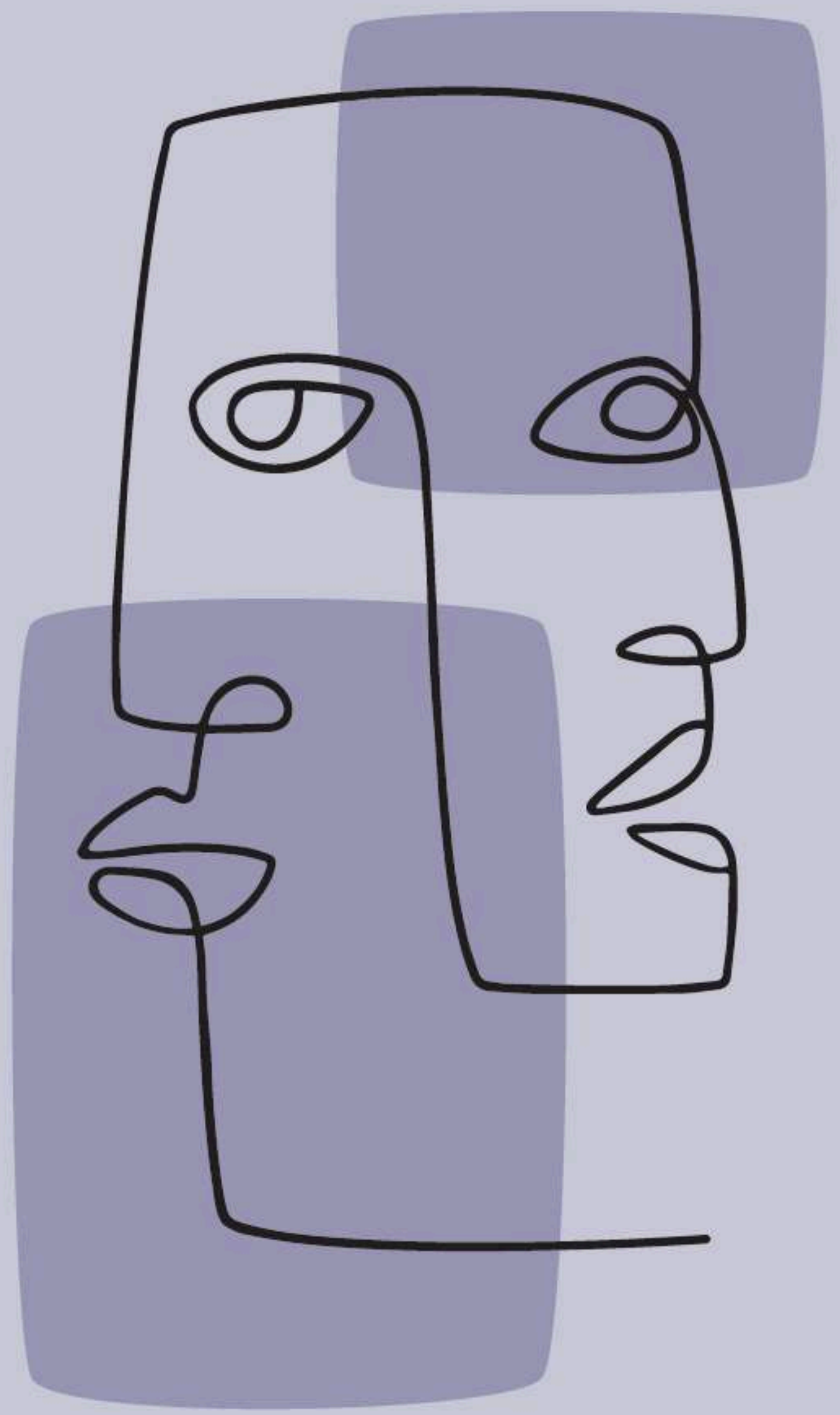


Figure 8.12: Details of node position in the lower jaw

Upper: mentoplate

Lower: facemask



SECTION 5: General discussion and summary

CHAPTER 9:

Discussion and Future perspectives

DISCUSSION

This doctoral thesis examined factors influencing the success of early treatment of skeletal Class III malocclusion through four interconnected research sections. The findings challenge several common assumptions about treatment approaches while highlighting the complexity of predicting individual outcomes.

Interceptive treatment for Class III malocclusion is reserved for cases with a skeletal component. One challenge with the term "Class III malocclusion" is that it only describes the occlusal relationship, without specifying the underlying causes—whether dental, skeletal, functional, or any combination thereof. In the literature, the terms "true Class III" and "functional (or pseudo-) Class III" are commonly used to differentiate skeletal from dental Class III malocclusions.

The characteristics of adult skeletal Class III malocclusion have been thoroughly documented and compared with normal or Class I occlusion. However, the criteria for pseudo-Class III malocclusion remain poorly defined, particularly regarding its dentoskeletal features in the early mixed dentition [1]. It is also difficult to identify clinical signs in a growing child that might indicate an emerging Class III growth pattern [2]. Indeed, some young patients with Class III malocclusion may exhibit a skeletal Class I relationship, whereas others with a skeletal Class III relationship can present with a normal overjet and overbite [2]. Moreover, Class III malocclusion often worsens over time as growth progresses [3,4],yet at early stages, a skeletal pattern may not be clearly evident [5,6].

Distinguishing between dental and skeletal Class III malocclusions in children is most reliably accomplished through clinical evaluation, supplemented by radiographic analysis. Cephalometric assessment can aid in early diagnosis, but it should be part of a comprehensive approach that accounts for multiple developmental factors. Regular follow-up is critical for recognizing evolving growth patterns, leading to timely detection of skeletal Class III malocclusion.

In our study, we only included Class III cases with a pronounced skeletal component. This is demonstrated by the baseline cephalometric values presented in Chapter 5, showing a mean ANB of –0.69 (± 1.75) and a mean Wits appraisal of –5.67 (± 2.06).

In the third chapter, the systematic review revealed insufficient evidence regarding the long-term effects and stability of skeletal anchorage in interceptive Class III treatment. While bone anchors showed potential for better short-term skeletal effects with fewer dental compensations, the review highlighted a critical lack of high-quality long-term studies. This gap in the literature provided the foundation for our subsequent research.

In the fourth chapter, a multicenter retrospective analysis of 218 patients found that bone-anchored maxillary protraction (BAMP) was effective, but the skeletal changes observed were less pronounced than previously reported. The miniplate survival rate was 93.6%, with 25.7% of patients experiencing failure of at least one miniplate. This study underscored the importance of surgical technique and patient age in achieving successful treatment outcomes, while also suggesting that the presumed advantages of skeletal anchorage might not always translate into superior clinical results. Although this analysis reflects real-life clinical practice, several limitations should be recognized.

1. **Retrospective Study Design**: As a retrospective analysis, the study is susceptible to selection bias and information bias. It relied on existing medical records and radiographs, which could have been incomplete or inconsistent across different centers.
2. **Limited Cephalometric Data**: Although cephalometric analysis was performed on pre- and post-treatment radiographs, these were available for only 52 of the 218 patients (23.9%), substantially reducing the statistical power for evaluating skeletal changes. Additionally, no long-term follow-up data were available to assess the stability of treatment results.
3. **Multicenter Variability**: Although the multicenter, multi-surgeon, and multi-orthodontist context reflects real-world clinical settings, it introduces variability in surgical techniques, postoperative care, and orthodontic

management. These factors may have influenced outcomes. The significant variation in failure rates among centers further highlights this concern.

4. **Lack of Control Group**: The absence of a control group, either untreated Class III patients or those treated with alternative methods (e.g., facemask therapy), makes it difficult to distinguish the actual treatment effect of BAMP from natural growth changes.
5. **Unrecorded Compliance**: Patient compliance with elastic wear was not systematically documented, potentially affecting treatment outcomes.

In **chapters 5 and 6**, our randomized controlled trial comparing facemask and mentoplate protocols provided the first long-term comparative evidence between these approaches. The results showed comparable efficacy between traditional and bone-anchored treatments, with no significant differences in cephalometric and three-dimensional skeletal changes at both one-year and five-year follow-up. This challenges the assumption that more invasive bone-anchored treatments necessarily provide better outcomes.

At the time this study was initiated and the treatment protocol was defined (2016), there was ongoing debate regarding whether the Alt-RAMEC protocol could produce a greater skeletal effect. At that time, some evidence supported the idea that facemask therapy with dental anchorage might benefit from the Alt-RAMEC protocol. These findings were later confirmed in a 2020 systematic review by Wu et al [7.].

It appears that the Alt-RAMEC protocol can lead to faster and more pronounced skeletal effects in the short term when used with facemask therapy without skeletal anchorage, compared to conventional RME [8,9]. However, the quality of evidence supporting this is low. As outlined in Chapter 4, we did not find strong evidence at the time to support improved anchorage with the use of mini-screws in the upper jaw. Given our uncertainty about whether mini-screws could offer reliable skeletal anchorage (Chapter 4), we chose to apply the Alt-RAMEC protocol in both treatment groups in 2016.

More recent evidence, however, suggests that when mini-screws are used for anchorage in the upper jaw, the Alt-RAMEC protocol does not provide additional or faster skeletal effects in either the short or long term [10,11]. Based on this, we no longer recommend the use of the Alt-RAMEC protocol in combination with the hybrid hyrax appliance.

Nonetheless, when treatment is initiated at a later age (e.g., adolescence, 12–13 years), the Alt-RAMEC protocol may help compensate for the delayed timing. Therefore, its use should still be considered in such cases [12].

In chapters 7 and 8, we tried to identify predictive factors that could help identify outcome success before treatment started. The five-year follow-up study comparing facemask versus mentoplate therapy yielded surprising results. Traditional facemask therapy proved to be moderately more effective than mentoplate therapy in preventing the need for orthognathic surgery (81% vs 69% success rate), although these differences were not statistically significant. Previously proposed cephalometric predictive factors showed no correlation with final treatment outcomes, challenging the reliability of current prediction methods. The biomechanical modeling in chapter 8, investigated the possible use of patient-specific finite element models as a prediction tool. This revealed that while such models can help understand force distribution, they cannot reliably predict clinical outcomes. The consistent discrepancy between predicted and actual deformations suggests that successful prediction models must incorporate biological and growth factors beyond pure biomechanics.

POTENTIAL CLINICAL IMPLICATIONS

These results have several potential implications for clinical practice:

1. The choice between traditional and bone-anchored approaches should be based on individual patient factors rather than on perceived mechanical advantages. The current study found no additional therapeutic effect associated with the use of bone anchors. Despite widespread claims in

existing literature regarding their mechanical advantages, this investigation does not support the notion that bone anchors inherently enhance treatment outcomes. Therefore, clinicians should reconsider the routine assumption that bone anchors universally yield superior results. Treatment decisions should instead prioritize individual patient factors, including patient and parental preferences, compliance, anatomical considerations, and oral hygiene status.

2. Patient characteristics appear to be more influential in determining outcomes than the treatment method. The term "patient characteristics" in this context does not denote any single specific trait or cephalometric measurement. Rather, it underscores that the success or failure of treatment outcomes is predominantly influenced by intrinsic patient factors, such as individual growth patterns, rather than by the choice of orthodontic technique alone. This thesis did not identify any particular patient characteristics predictive of treatment success or failure. Therefore, clinicians are advised to evaluate treatment effectiveness after six months. If there is insufficient therapeutic progress—such as inadequate correction of Class III malocclusion—clinicians should critically reassess the treatment approach and consider terminating interceptive procedures in favor of an orthognathic surgical plan.

3. Current predictive tools, including cephalometric measurements and biomechanical models, demonstrate limited reliability in accurately predicting individual treatment outcomes. While caution is advised given that no other finite element model (FEM), aside from our simplified version, has been applied to the same patient sample, our FEM results were consistent with deformation patterns along the x-, y-, and z-axes reported in previous FEM studies [22–25], as noted in the Discussion section. There is little justification in applying a different FEM that models the same deformation patterns, as it would likely produce similar outcomes. Our aim was not to claim that force

distribution prediction is impossible; rather, we concluded that FEM alone is not suitable for predicting overall treatment outcomes.

4. Although early intervention significantly reduces the need for surgery, clinicians should counsel patients that approximately 25-30% may require orthognathic surgery despite successful initial treatment. This conclusion is derived from the analysis presented in Chapter 7 and aligns with previously reported long-term outcomes for both facemask and bone-anchored treatment protocols [13,14].

5. The following figures illustrate clinical cases demonstrating treatment outcomes using a facemask appliance (figures 9.1 – 9.3) and a mentoplate appliance (figures 9.4 – 9.6).

Figure 9.1: clinical, intra-oral and cephalometric images of 8-year-old girl at start of facemask treatment.

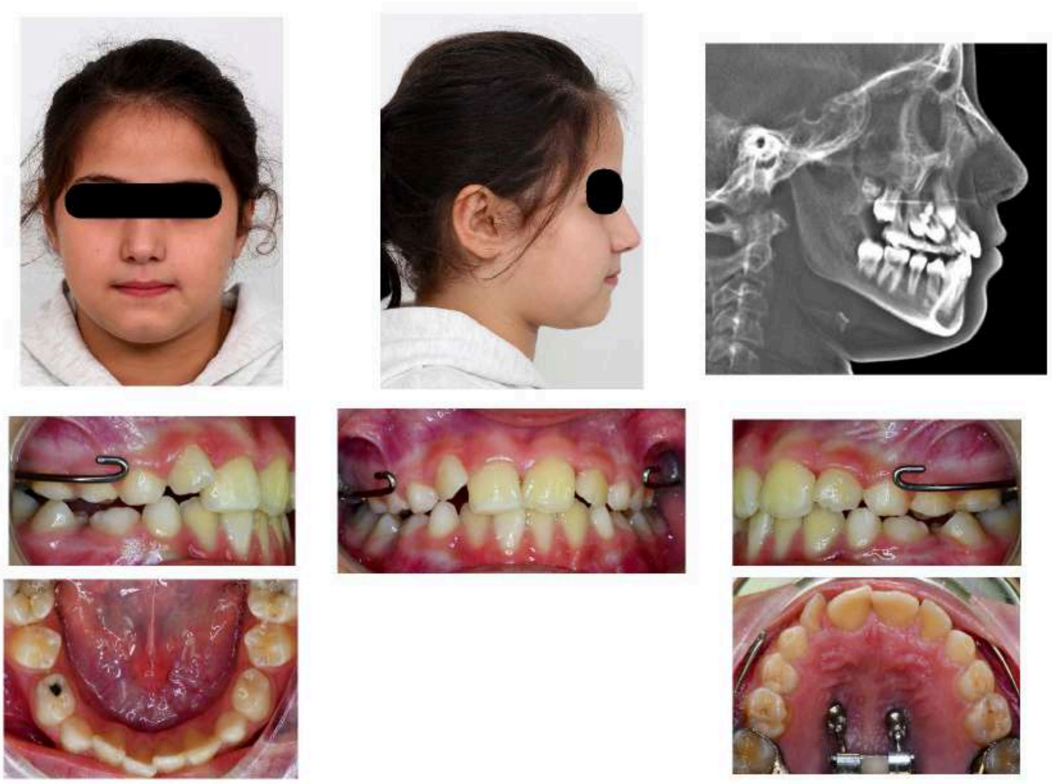


Figure 9.2: clinical, intra-oral and cephalometric images of 9-year-old girl 13 months after start facemask treatment

Figure 9.3: clinical, intra-oral and cephalometric images of 14-year-old girl 66 months after start facemask treatment

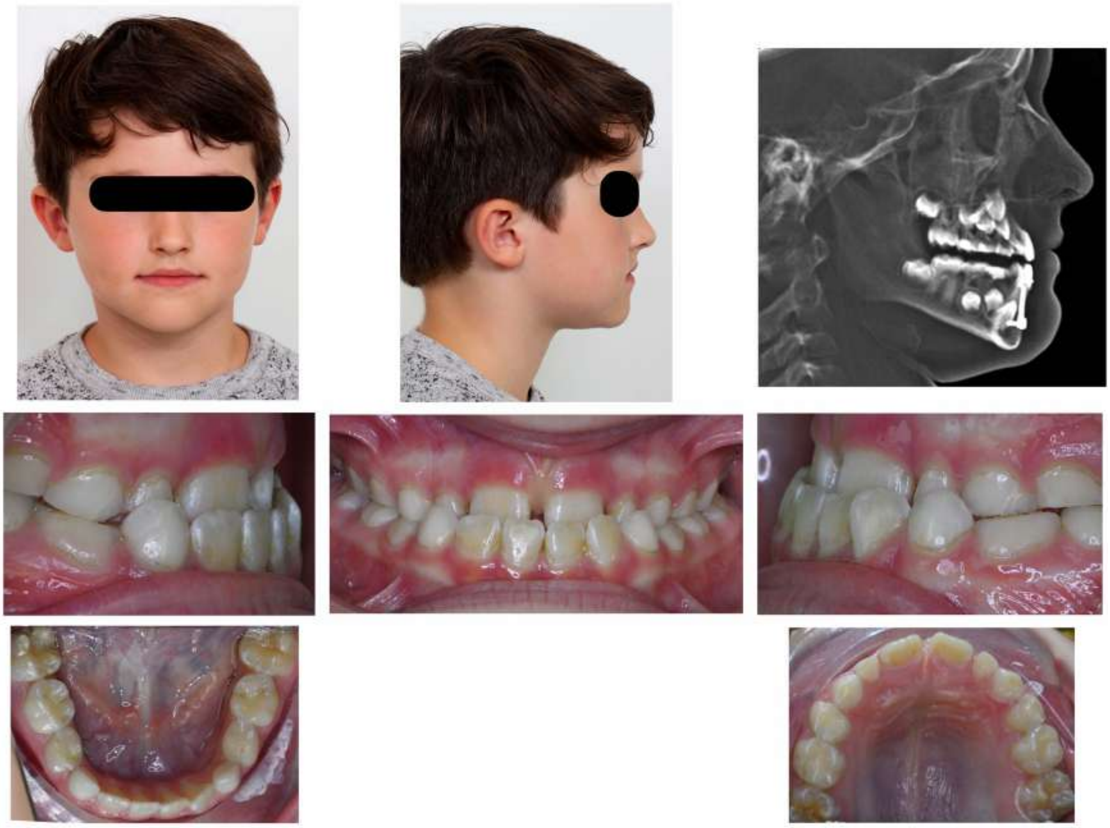


Figure 9.4: clinical, intra-oral and cephalometric images of 8-year-old boy at start of mentoplate treatment.

Figure 9.5: clinical, intra-oral and cephalometric images of 9-year-old boy 13 months after start mentoplate treatment

Figure 9.6: clinical, intra-oral and cephalometric images of 14-year-old boy 64 months after start mentoplate treatment

METHODOLOGICAL LIMITATIONS

This thesis is limited by several methodological limitations that affect the reliability of its findings and conclusions.

Sample Size and population: first, the RCT included relatively small groups (n=28), although this sample size is common in long-term orthodontic studies. Secondly, the study population was predominantly Caucasian, which may limit generalisability to other ethnic groups. Finally, patient dropout at the five-year follow-up reduced the final sample size.

Study Design: firstly, the lack of an untreated control group in the clinical trials due to ethical considerations. This made it difficult in distinguishing between treatment effects and natural growth changes. Secondly, the inability to blind operators and patients to treatment allocation. Finally, the variation in timing and duration of treatment between patients.

CONCLUSION

This thesis demonstrates that successful early Class III treatment depends more on individual patient characteristics than on the specific treatment approach chosen. While both traditional and bone-anchored techniques can effectively reduce the need for future surgery, neither approach guarantees long-term success. Future research should focus on developing better predictive tools that incorporate multiple factors to guide clinical decision-making.

FUTURE PERSPECTIVES

The results of this doctoral thesis open up several promising avenues for future research in the early treatment of Class III malocclusions.

The limitations of current prediction methods highlight the need for more sophisticated approaches. Future research should focus on the development of integrated prediction models that combine multiple sources of data. These could include traditional cephalometric measurements, three-dimensional imaging data, genetic markers, and biological indicators of growth potential. Machine learning algorithms could be particularly valuable in processing these complex datasets to identify subtle patterns that might predict treatment success. Such comprehensive models could revolutionize our ability to identify patients most likely to benefit from early intervention.

While 3D volumetric analysis complements traditional 2D cephalometric measurements, the overall changes detected in the maxilla and mandible are minimal. These subtle volumetric differences make it difficult to effectively compare treatments and are difficult for clinicians to understand. Future research should investigate specific anatomical structures and soft tissue changes, requiring new validated registration tools and a more comprehensive and standardized outcome analysis.

The field would benefit from larger, multi-center randomized controlled trials that follow patients through to full skeletal maturity. These trials should include standardized treatment protocols across centers, diverse patient populations to improve generalizability, comprehensive outcome measures including patient-reported outcomes, economic analyses to assess cost-effectiveness, quality of life assessments before, during, and after treatment, and long-term follow-up extending well into adulthood. Such trials would provide more definitive evidence on the comparative effectiveness of different treatment approaches and help identify factors that influence long-term stability.

REFERENCES

1. Rabie AB, Gu Y. Diagnostic criteria for pseudo-Class III malocclusion. *Am J Orthod Dentofacial Orthop*. 2000;117(1):1-9. doi:10.1016/S0889-5406(00)70241-1
2. Williams S, Andersen Aarhus CE. The morphology of the potential Class III skeletal pattern in the growing child. *Am J Orthod*. 1986;89(4):302-311. doi:10.1016/0002-9416(86)90052-7
3. Baccetti T, Reyes BC, McNamara JA. Craniofacial changes in Class III malocclusion as related to skeletal and dental maturation. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2007;132(2):171.e1-171.e12.
4. Kuc-Michalska M, Baccetti T. Duration of the pubertal peak in skeletal class I and Class III subjects. *Angle Orthodontist*. 2010;80(1):54-57. doi:10.2319/020309-69.1
5. Jacobson A, Evans WG, Preston CB, Sadowsky PL. Mandibular prognathism. *Am J Orthod*. 1974;66(2):140-171. doi:10.1016/0002-9416(74)90233-4
6. Guyer EC, Ellis EE, McNamara JA, Behrents RG. Components of class III malocclusion in juveniles and adolescents. *Angle Orthod*. 1986;56(1):7-30.
7. Wu Z, Zhang X, Li Z, et al. A Bayesian network meta-analysis of orthopaedic treatment in Class III malocclusion: Maxillary protraction with skeletal anchorage or a rapid maxillary expander. *Orthod Craniofac Res*. 2020;23(1):1-15.
8. Pithon MM, De N, Santos L, et al. Is alternate rapid maxillary expansion and constriction an effective protocol in the treatment of Class III malocclusion? A systematic review Is alternate rapid maxillary expansion and constriction protocol effective in the treatment of Class III maloc- c. *Dental Press J Orthod Dental Press J Orthod Dental Press J Orthod*. 2016;212121(666):34-4234.
9. Almuzian M, McConnell E, Darendeliler MA, Alharbi F, Mohammed H. The effectiveness of alternating rapid maxillary expansion and constriction combined with maxillary protraction in the treatment of patients with a class III malocclusion: a systematic review and meta-analysis. *J Orthod*. 2018;45(4):250-259. doi:10.1080/14653125.2018.1518187
10. Masucci C, Franchi L, Franceschi D, Pierleoni F, Giuntini V. Post-pubertal effects of the Alt-RAMEC/FM and RME/FM protocols for the early treatment of Class III malocclusion: A retrospective controlled study. *Eur J Orthod*. 2022;44(3):303-310.
11. Ergul T, Gulec A. Comparison of the effectiveness of skeletal and tooth-borne protraction methods with or without alternate rapid maxillary expansion and constriction protocol in patients with Class III malocclusion. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2024;article in. doi:10.1016/j.ajodo.2024.10.010
12. Papadopoulou AK, Koletsi D, Masucci C, Giuntini V, Franchi L, Darendeliler MA. A retrospective long-term comparison of early RME-facemask versus late Hybrid-Hyrax, alt-RAMEC and miniscrew-supported intraoral elastics in growing Class III patients. *Int Orthod*. 2022;20(1):100603.
13. Mandall N, Cousley R, Dibiase A, et al. Early class III protraction facemask treatment reduces the need for orthognathic surgery: a multi-centre, two-arm parallel randomized, controlled trial. *J Orthod*. 2016;43(May 2017):164-175.
14. Mandall N, Aleid W, Cousley R, et al. The effectiveness of bone anchored maxillary protraction (BAMP) in the management of class III skeletal malocclusion in children aged 11–14 years compared with an untreated control group: A multicentre two-arm parallel randomised controlled trial. *J Orthod*. Published online 2024. doi:10.1177/14653125241255139

SUMMARY

This thesis manuscript explores the effectiveness of different treatment approaches for Class III malocclusion (underbite) in growing patients. The research is structured in three main sections:

Section 2 assessed the efficacy of bone anchors through systematic review and clinical practice analysis, finding that bone anchors, despite being more invasive, don't necessarily produce better treatment effects than traditional approaches.

Section 3 reports on a 5-year randomized controlled trial comparing facemask (FM) versus mentoplate (MP) treatment protocols, showing that both treatments were similarly effective. Comprehensive analysis of treatment outcomes using both 2D and 3D measurements, challenge the common assumption that bone-anchored treatments necessarily provide better results than traditional approaches.

Section 4 investigated treatment outcome prediction using both 2D and 3D analysis, revealing that patient characteristics may be more influential than treatment type, and that current prediction models have significant limitations. Traditional facemask therapy was slightly more effective at preventing future orthognathic surgery (81% vs 69%), although this difference was not statistically significant.

To summarize, the choice between traditional and bone-anchored approaches should be based on individual patient factors rather than assumed mechanical advantages, as the effectiveness of treatment appears more dependent on patient characteristics than the specific technique used. About 25-30% of treated patients may still require surgery despite early intervention. Current predictive models are insufficient for reliable treatment planning.

SAMENVATTING

Dit proefschrift onderzoekt de effectiviteit van verschillende behandelmethoden voor Class III malocclusie (onderbeet) bij groeiende patiënten. Het onderzoek is opgedeeld in drie hoofdsecties:

Sectie 2 beoordeelde de effectiviteit van botankers via een systematische review en een analyse van de klinische praktijk. Hieruit bleek dat botankers, ondanks hun invasieve aard, niet per se betere behandelresultaten opleveren dan traditionele methoden.

Sectie 3 rapporteert over een 5-jarige gerandomiseerde gecontroleerde studie waarin facemask (FM)- en mentoplate (MP)-behandelingen met elkaar werden vergeleken. Beide behandelingen bleken even effectief. Een uitgebreide analyse van de behandelresultaten met zowel 2D- als 3D-metingen daagt de gangbare aanname uit dat botverankerde behandelingen noodzakelijkerwijs betere resultaten opleveren dan traditionele methoden.

Sectie 4 onderzocht de voorspellende waarde van behandelings-resultaten met behulp van zowel 2D- als 3D-analyse. De resultaten suggereren dat patiënt-kenmerken een grotere invloed hebben dan het type behandeling en dat de huidige voorspellings-modellen aanzienlijke beperkingen vertonen. Traditionele facemask-therapie was iets effectiever in het voorkomen van toekomstige orthognatische chirurgie (81% versus 69%), maar dit verschil was niet statistisch significant.

Conclusie: De keuze tussen traditionele en botverankerde behandelingen zou gebaseerd moeten zijn op individuele patiëntkenmerken in plaats van op veronderstelde mechanische voordelen. De effectiviteit van de behandeling lijkt meer afhankelijk te zijn van de eigenschappen van de patiënt dan van de toegepaste techniek. Ongeveer 25-30% van de behandelde patiënten zal ondanks vroege interventie nog steeds een operatie nodig hebben. De huidige voorspellingsmodellen zijn onvoldoende betrouwbaar voor nauwkeurige behandelplanning.

PERSONAL CONTRIBUTION

Joeri Meyns conceptualized, planned, asked for ethical approval, organized and carried out the experiments, interpreted the results and wrote the manuscripts presented in this thesis in consultation with the supervisors and co-authors listed in the respective chapters and mentioned under scientific acknowledgements.

CONFLICT OF INTEREST

The author of this doctoral thesis has no conflict of interest to declare.

USE OF GENERATIVE AI

I did not use generative AI assistance tools during the research/writing process of my thesis, except for mere language assistance. The text/code/ images in this thesis are my own and generative AI has only been used in accordance with the KU Leuven guidelines and appropriate references have been added. I have reviewed and edited the content as needed and I take full responsibility for the content of the thesis.

SCIENTIFIC AKNOWLEDGEMENTS

This thesis was the result of a collaborative effort on each chapter. I would like to mention the people who made scientific contribution to each of the present studies. I am grateful to each of you.

Aerts Johan: Performed orthodontic treatment of study patients in section 4, clinical data collection and helped conceptualizing the treatment protocols. He also provided valuable insights to chapter 9.

Brasil Daniele: Systematic review methodology, data collection and analysis (Chapter 3).

Claeys Thomas: Data collection and analysis for bone anchor efficacy study (Chapter 4).

Dons Flore: Clinical data collection and analysis (Chapter 9) and preparing the schematic cephalometric figures. She also contributed to the writing of the article in chapter 9.

Jacobs Reinhilde: Established project foundation and provided comprehensive supervision of thesis development. Offered methodological guidance, revised manuscripts (all chapters), and facilitated collaborative partnerships. Maintained supportive mentorship throughout the project, ensuring its successful completion.

Jazil Omid: Data collection and analysis for 3D assessment studies (Chapter 7) and co-writing of the paper in this chapter. Data collection and analysis for prediction studie (Chapter 5)

Jindanil Thanatchaporn: Conducted data collection and statistical analysis for long-term assessment studies, creating figures for final reports (Chapters 5 and 8)

Mazzi-Chaves Jardel: Systematic review methodology and analysis (Chapter 3)

Meewis Jeroen: Clinical data collection and analysis (Chapter 5 and 9). He also contributed to the writing of the article in chapter 9.

Nout Erik: Data collection and analysis for bone anchor efficacy study (Chapter 4). Contributed to the writing and proof-reading of the article in chapter 4.

Politis Constantinus: He closely followed-up on the progress of this thesis and papers. His understanding of facial growth and extensive clinical experience provided valuable insights, substantially improving the quality of the present project.

Scheerlinck Jan: Clinical data collection and analysis (Chapter 4). Contributed to the writing and proof-reading of the article in chapter 4.

Schreurs Arnoud: Conducted orthodontic treatment of study patients, collected clinical data, and helped develop treatment protocols. Contributed clinical expertise to Chapter 9 and provided the majority of clinical photographs for this thesis.

Shujaat Sohaib: He contributed significantly to the 3D analysis methodology, data collection, and interpretation across multiple chapters. His role included co-writing and proofreading papers in chapters 5, 6, 7, 8, and 9. His invaluable input in rewriting, interpreting statistical results, and reporting outcomes was of immeasurable importance.

Van Caesbroeck Kato: Data collection and analysis for prediction studie (Chapter 5)

Van Cauter Sofie: Biomechanical modeling and analysis (Chapter 6), Facilitating and providing accessibility to CT-graphic examinations.

Van Hevele Jeroen: Lead author for bone anchor efficacy study (Chapter 4)

Vander Sloten Jos: Biomechanical modeling supervision and analysis (Chapter 6).

Vertenten Wout: Biomechanical modeling and data analysis (Chapter 6). He also contributed to the writing of the article in this chapter

CURRICULUM VITAE

Joeri MEYNS, MD, DMD

joerimeyns@outlook.com
joeri.meyns@zol.be

Joeri Meyns was born in Oostende, Belgium, on June 30, 1979. He obtained his medical degree (KU Leuven, *magna cum laude*) in July 2004, followed by his dental degree (KU Leuven, *magna cum laude*) in July 2007.

In 2007, he began his residency in oral and maxillofacial surgery at Ziekenhuis Oost-Limburg (Genk, Belgium). His training included rotations in general and orthopedic surgery at Sint-Trudo Ziekenhuis (Sint-Truiden, Belgium) and further specialization in oral and maxillofacial surgery at ETZ Elisabeth Hospital (Tilburg, Netherlands) and the University Hospitals of Leuven (Belgium).

From 2011 to 2014, Dr. Meyns served as a staff member at Maastricht University Medical Center (MUMC, Netherlands), where he further specialized in oncologic and reconstructive surgery. In 2014, he joined Ziekenhuis Oost-Limburg (Genk, Belgium) as a full-time consultant with a focus on orthognathic and reconstructive surgery.

Between 2017 and 2019, he was responsible for training oral and maxillofacial surgery residents at ZOL. In 2019, he was appointed Clinical Head of the Oral and Maxillofacial Surgery Department in Genk, a role that expanded in 2022 to include the department in Maaseik. That same year, he co-founded and became the Clinical Director of the 3D Printing Lab at ZOL (Genk).

Dr. Meyns pursued his doctoral research from 2018 to 2025 within the OMFS-IMPATH research group at KU Leuven, supervised by Prof. Dr. Reinhilde Jacobs and Prof. Dr. Constantinus Politis. His research concentrated on growth modification strategies for children presenting with skeletal Class III malocclusion.

He is a wine enthusiast with a strong focus on locally produced wines. After completing a three-year training program in vineyard work and winemaking, he obtained his degree in the field. Since then, he has planted a small vineyard where he produces his own wines.

CLINICAL POSITIONS

- 2011- ‘14 Consultant oral and maxillofacial surgery
  MUMC (Maastricht, The Netherlands)

- 2013- ….: Consultant oral and maxillofacial surgery
  Ziekenhuis Oost Limburg (Genk, Belgium)

- 2017- ‘19: Stagemeester oral and maxillofacial surgery
  Ziekenhuis Oost Limburg (Genk, Belgium)

- 2019- ….: Head of department oral and maxillofacial surgery
  Ziekenhuis Oost Limburg (Genk, Belgium)

- 2022- ….: Head of department oral and maxillofacial surgery
  Ziekenhuis Oost Limburg (Maaseik, Blegium)

RESEARCH POSITIONS

- 2019 - ‘25: PhD OMFS IMPATH
  KULeuven (Belgium)
  Growth modification in children with Class III malocclusion.
  Promotor: Prof. Dr. R. Jacobs
  Co-promotor: Prof. Dr.. C. Politis

EDUCATION

- 1997- 00: Bachelor of Science in Medicine
  KULAK (Kortrijk, Belgium)

- 2000- ’04: Master of Science in Medicine
  KU Leuven (Belgium)

- 2003- ’07: Master of Science in Dentistry
  KU Leuven (Belgium)

- 2004- ’05: United states medical licensing examination: step 2 CK

- 2006- ‘07 Micro-surgical course (Centre Surgical Technologies)
  KU Leuven (Belgium)

- 2007- ‘08 Resident Oral and Maxillofacial Surgery (Prof. Dr. Politis)
  ZOL Genk (Belgium)

- 2008- ‘09 Resident General Surgery (Dr. Geyskens)
  Orthopedic Surgery (Dr. Renson)
  ENT-Surgery (Dr. Annys)
  St Trudo hospital Sint-Truiden (Belgium)

- 2009- ’10 Resident Oral and Maxillofacial Surgery (Dr. Scheerlinck) **ETZ Elisabeth Hospital (Tilburg, Netherlands)**

- 2010 - ’11 Resident Oral and Maxillofacial Surgery (Prof. Dr. Schoenaers) **UZ Leuven (Belgium)**

- 2021 – ‘23 Vineyard work and Winemaking (G. Van Rennes) **Syntra (Belgium)**

INVITED LECTURES

25/02/2025 Tandheelkundige Kring Oostende (Belgium)
Klasse III behandeling bij het jonge kind

13/02/2025 BUOS 2025, Brussel (Belgium)
Class III correction in the young child: “to anchor or not to anchor?

26/04/2024 VVT (kempen), Kasterlee (Belgium)
Dynamic navigation in implantology
“Guiding the future or navigating complexity?”

02/10/2021 Emeriti conference Dr. Wuyts, Zolder (Belgium)
Brughoektumoren en microvasculaire decompressie

26/03/2021 NVVO, Soestduinen (The Netherlands)
Class III correction in the young child.

21/09/2019 LOK, Leuven (Belgium)
Verankering en distractoren in de orthognatische heelkunde

18/05/2019 VVT- MKA, Antwerp (Belgium)
Klasse III behandeling bij het jonge kind

24/02/2018 Symposium KNO, Genk (Belgium)
Quality of life na tumor-behandeling in de mondholte.

LIST OF PUBLICATIONS

1. Böckmann R, Schön P, Neuking K, **Meyns J**, Kessler P, Eggeler G. In vitro comparison of the sagittal split osteotomy with and without inferior border osteotomy. J Oral Maxillofac Surg. 2015 Feb;73(2):316-23.
2. Böckmann R, **Meyns J**, Dik E, Kessler P. The modifications of the sagittal ramus split osteotomy: a literature review. Plast Reconstr Surg Glob Open. 2015 Jan 8;2(12): 271.
3. Lie N, Merten HA, **Meyns J**, Lethaus B, Wiltfang J, Kessler P. Elevation of the maxillary sinus membrane for de-novo bone formation: First results of a prospective study in humans. J Craniomaxillofac Surg. 2015 Oct;43(8):1670-7.
4. **Meyns J.**, Brasil D.M., Mazzi-Chaves J.F., Politis C., Jacobs R. The clinical outcome of skeletal anchorage in interceptive treatment (in growing patients) for class III malocclusion: a systematic review. *Int J Oral Maxillofac Surg 2018; 47: 1003–1010*
5. Van Hevele J, Nout E, Claeys T, **Meyns J**, Scheerlinck J, Politis C. Bone-anchored maxillary protraction to correct a class III skeletal relationship: A multicenter retrospective analysis of 218 patients. *Journal of cranio-maxillofacial Surgery 2018; 46: 1800-180*
6. Ockerman A, Miclotte I, Vanhaverbeke M, Vanassche T, Belmans A, Vanhove J, **Meyns J**, Nadjmi N, Van Hemelen G, Winderickx P, Jacobs R, Politis C, Verhamme P. Tranexamic acid and bleeding in patients treated with non-vitamin K oral anticoagulants undergoing dental extraction: The EXTRACT-NOAC randomized clinical trial. PLoS Med. 2021 May 3;18(5): 1003601.
7. Ver Berne J, Politis C, **Meyns J**, Li J, Jacobs R. Prevalence of systemic conditions in an orthognathic surgery population: A 20-year single-center study. Oral Surg Oral Med Oral Pathol Oral Radiol. 2022 Aug;134(2):163-167.
8. Garip L, Verbist J, Stragier H, **Meyns J**, Mesotten D, Vundelinckx J. A comparative study of patient satisfaction about anesthesia with dexmedetomidine for ambulatory dental surgery. BMC Res Notes. 2022 Dec 22;15(1):376.

9. Jindanil T, Burlacu-Vatamanu OE, **Meyns J**, Meewis J, Automated orofacial virtual patient creation: A proof of concept. J Dent. 2024 Nov;150:105387. doi: 10.1016/j.jdent.2024.105387. Epub 2024 Oct 2. PMID: 39362299.
10. Jindanil T, Burlacu-Vatamanu OE, Baldini B, **Meyns J,** Meewis J, Fontenele RC, Perula MCL, Jacobs R. Automated orofacial virtual patient creation using two cohorts of MSCT vs. CBCT scans. Head Face Med. 2025 Mar 28;21(1):21. doi: 10.1186/s13005-025-00500-1. PMID: 40156051; PMCID: PMC11951535.
11. **Meyns J**., Meewis J., Dons F., Schreurs A., Aerts J., Shujaat S, Politis C., Jacobs R. Long-term Comparison of Maxillary Protraction with Hybrid Hyrax-Facemask vs Hybrid Hyrax-Mentoplate Protocols Using Alt-RAMEC: A 5-Year Randomized Controlled Trial. *European Journal of Orthodontics, 47(2), April 2025.*
12. **Meyns J.**, Jindanil T., Shujaat S., Politis C., Jacobs R. Long-term Three-dimensional Skeletal Effects of Hybrid Hyrax with Facemask versus Mentoplate in Growing Class III Patients: A Randomized Controlled Trial. *Progress in Orthodontics, 26 (14) April 2025*